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FEBRUARY 1965

FLUID BALANCE AND ELECTROLYTE DISTRIBUTION IN THE HUMAN BODY

Edward C. DeLand and Gilbert B. Bradham

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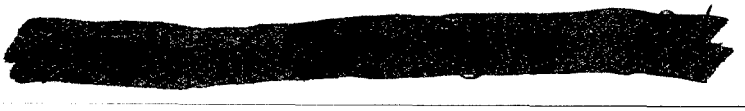

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PREFACE

This Memorandum concerns the general problem of computing the distribution of chemical species in a well-defined biological subsystem at steady state. As such, it is one of a series of studies by various authors (see bibliography for a partial listing) at The RAND Corporation relating to the same area of biochemical research.

In particular, we show here a mathematical method for computing the fluid and electrolyte distribution in simultaneous subcompartments of the human body at rest and under various stresses. This amounts to a mathematical model of the subsystem which can be used, with specific reservations, to predict the results of clinical and laboratory experiments and to deduce the state of experimentally unavailable human subcompartments.

Although several such mathematical experiments are discussed, the model described in this report should be regarded as an interim stage in the development of a sufficiently complex research model of the whole body fluid and electrolyte balance.

The coauthor, Dr. Gilbert B. Bradham, is a consultant to The RAND Corporation. At the time of this research,

Dr. Bradham was a National Institutes of Health Fellow at the School of Medicine, Department of Surgery, University of California at Los Angeles. Now he is at the Medical College Hospital of the Medical College of South Carolina.

SUMMARY

This Memorandum presents a conceptual model and a mathematical method for computing the physiological fluid and electrolyte distribution for selected body compartments of an average, young, 70-kilogram human male. The mathematical procedure simulates the physiological subsystems by incorporating all the known chemical reactions and electrochemical relations which seem necessary to establish the fluid and electrolyte distribution. Because the whole body is being considered, the relatively large number of computations required argues that a computer be employed.

The construction of the model and the mathematical background is given in heuristic form only, with reference to earlier papers for rigorous development. However, considerable detail is shown regarding the analysis of the computed results for a standard, steady-state, average, young, resting, 70-kg human male. Finally, the results of validation experiments, consisting of chemical stresses applied to the model, are discussed. In some cases, these results are compared with similar experiments in the biological literature, but in others reference is made to a

companion paper by G. B. Bradham, et al. [1], in which particular laboratory validation experiments are described in detail. The results of these experiments indicate that the model is a valid supplementary tool for research in the clinical and the research laboratory as well as in theoretical physiology.

ACKNOWLEDGMENTS

The antecedents of this paper lie in the work of many other people. It is one product of a cooperative research effort between The RAND Corporation and the School of Medicine, University of California, Los Angeles. The RAND participants are Richard Clasen, James C. DeHaven, Norman Shapiro, and the author. James V. Maloney, Jr. and Gilbert Bradham lead the University group.

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I. INTRODUCTION

In this Memorandum we present a conceptual model and a mathematical method for computing the fluid and electrolyte distribution for selected body compartments of an average, 70-kilogram human male. We will deal principally with a mathematical model simulating the healthy, resting, standard state. As will be shown, however, with adequate validation such a model can also be used to simulate the steady states which result from well-defined physical or chemical stresses.

Because we are dealing with the whole body* simultaneously, the relatively large number of computations required argues that a computer be employed, but in return for the possible inconveniences thus engendered, many subsidiary benefits are derived. In addition to the determination of fluid and electrolyte species distribution in a very large system, one has the ease of experimental variation and hypothesis testing; fast, inexpensive,

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*By the term "whole body," as used here, we mean, as in Moore [2, p. 19], the total of the "biochemical phases--fluids and solids--which constitute...the whole body: a gross, intact, functioning and living unit." But, we will examine, for now, only a selected subset of the total body, certain subcompartments as detailed below.

and accurate computation; and flexibility of the model on either the macroscopic mass distribution or the microscopic chemical reaction level.

It should be made clear at the outset that this mathematical model does not involve the degree of complexity of a total viable system. It is used, instead, to approximate the functions of certain systems by incorporating in one format all known or hypothetical chemical reactions and electrochemical relations which seem pertinent to that system--in this case, the fluid and electrolyte balances in the body. Further, the first approximate model need not be discarded when new details are added--it will merely grow in articulation, complexity, and, presumably, validity as hypotheses are tested, proven, and incorporated into the model.

An analytic model, just as a conceptual laboratory model, of a viable, homeostatic biological system is not as complex as the system and entails assumptions and compromises. Most such assumptions can be judiciously chosen and defined for the model, but often the assumptions are difficult to clarify or may even be covert. The resulting discrepancy between the model and the system may be significant, since it is a measure of the biological integrity and, hence, the usefulness of the model.

It is desirable, of course, to ameliorate the approximations of the model to the system by improving the model. But it is essential to emphasize the dependence of the model on reliable and detailed biological knowledge. The development of the model consists of fitting the system together piece by piece as the details are available in the biological literature and then verifying the results against laboratory experiment. Eventually, the same experiment is run in both facilities and each should predict the results of the other. When they do not, it is because either the experiments are not actually comparable or the biological data are invalid or inconsistent.

The mathematical model is, in this sense, an idealized experiment, in which the stated conditions and assumptions always hold. In the laboratory, however, the requirements for a new hypothesis, for example, can be stated; but in the actual experiment, the necessary conditions may be difficult to attain or difficult to hold, especially for extended periods.

We deal here with such an idealized experiment, but one which has become sufficiently complex and sufficiently complete as to have clinical interest and research possibilities. It will, however, be necessary to rationalize--

analytically if possible--the differences between the laboratory experiment and the model.

The particular mathematical model considered (called "Whole Body II") has shown sufficient promise and consistency to invite such clinical laboratory verification. In a companion paper, G. B. Bradham, et al. [1], of the University of California at Los Angeles School of Medicine, Department of Surgery, have discussed in detail the isotope method used and the comparison between the clinical laboratory and this mathematical model when the same experiment is run in both facilities. An "experiment" consists of applying normally expected chemical stresses to the mathematical model and to nephrectomized (kidney removed) dogs. Nephrectomized animals were chosen in a deliberate attempt to minimize certain transient side-phenomena, as will be discussed below. The results of this validation are summarized in Sec. VI.

Because of the inordinate complexity of whole-body laboratory experiments, much of the work in whole-body fluids and electrolytes has been pragmatic and empirical. The inaccessibility of some of the body compartments to direct measurement requires that rules of thumb be applied to account for rather complex phenomena--e.g., intracellular-

interstitial Gibbs-Donnan relations; also, a detailed theoretical explanation is often subordinate to more generalized but practical conclusions. A result is that the accumulated data and information are not necessarily relatable by consistent hypotheses or uniform conditions of experiment. Of course, there are an unusually large number of detailed problems related to laboratory work in this area; standards and controls are difficult to establish. But beyond these factors, the data are generally unrelatable and variable owing to the absence of an abstract theory, or model, or view, that is sufficiently complex and detailed for the task. Too many factors in the whole body must be organized and interrelated at one time. We will propose a unifying model and method which is at once simple and yet can be adequately detailed and comprehensive.

II. CONDITIONS, ASSUMPTIONS, STANDARDS, AND OBJECT OF STUDY

Conceptually, the body can be divided into various compartments, distinct in chemical content and yet related physically and chemically by communication across intervening membranes or other conceptual boundaries. Thus, we will be concerned with the following compartments:

I. The gaseous components of venous plasma;

II. The interiors, but not the membranes, of the red cells taken together as a compartment;

III. The plasma;

IV. The interstitial fluid;

V. The intracellular fluid of the body cell mass taken together as a compartment, not including red cells.

At this point, it is sufficient that the model be that of a nephrectomized animal; a kidney will be added later. The chemical content of the bones, the gut, the connective tissue, the neural and spinal fluid, and the muscle and red cell membranes, with which we are not now concerned, is taken to be constant.

Each compartment is taken to be uniform and homogeneous throughout (by which is meant that the diffusion processes within the compartment are not material, and mixing is

complete). A body "compartment" is thus used in the sense of Moore [2] and Edelman [3,4] where, for example, the body is conveniently divided into functionally separate, though interdependent, subdivisions, as for total body water in Fig. 1. We will make a further subdivision of Fig. I by separating the interior of the red cells from the intracellular compartment, and, of course, we will add the pertinent chemical species to each compartment.

The chemical compositions of the compartments I through V are, of course, variable with the state of the animal or the stress applied. We begin, however, with a standard reference state for the model which is well defined: a resting, young, male human. Later, during the laboratory verification experiments, we will refer to the clinically immobile, nephrectomized dog. The dog is a necessary compromise in order to investigate initially the qualitative aspects of the response of the human simulation to chemical stresses.

Specifically, the principal sources for standard data were Spector, Handbook of Biological Data [5] and Edelman, Anatomy of Body Water and Electrolytes [3]. Many secondary sources, to which specific reference will be made as appropriate, are listed in the References.

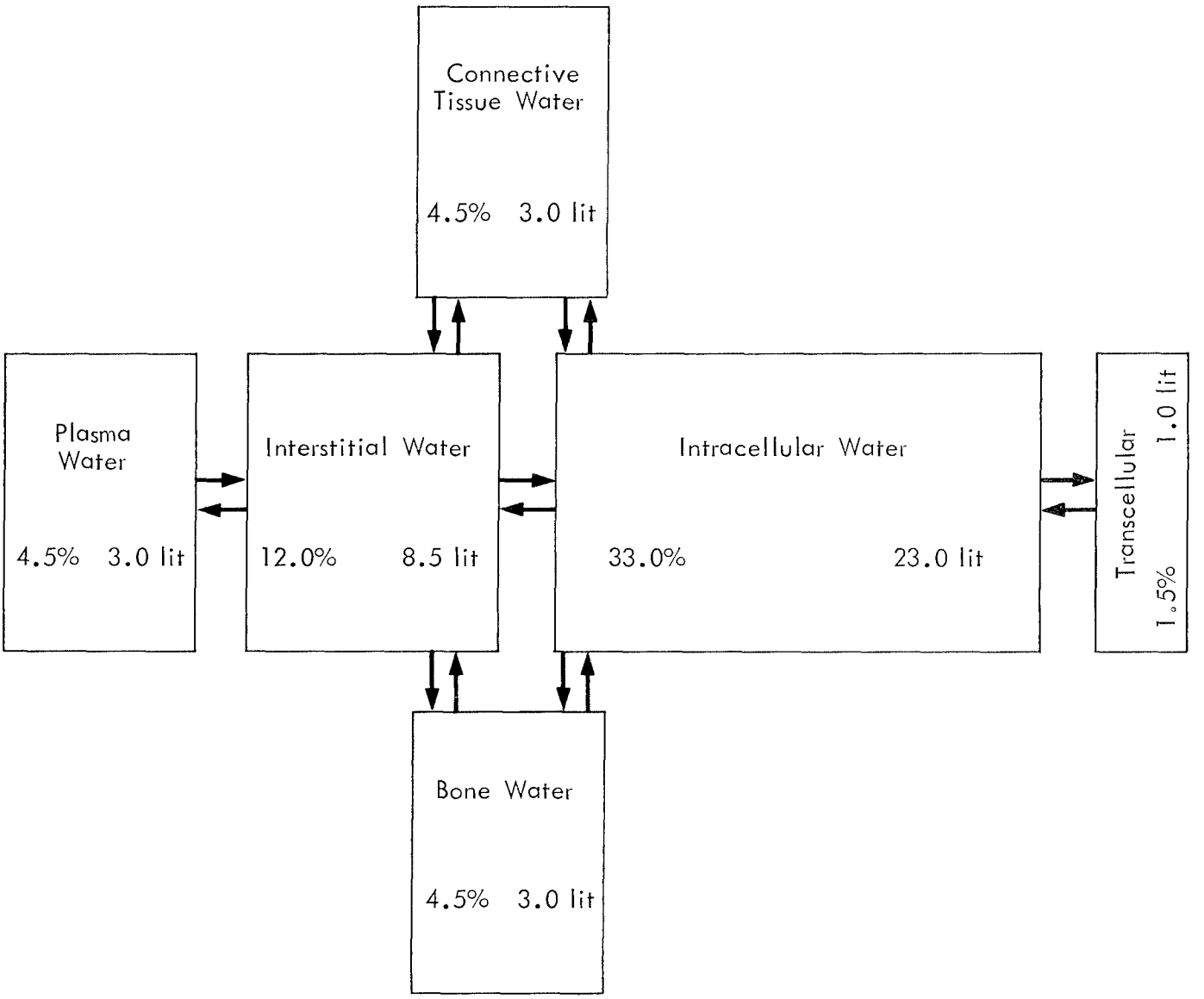


Fig. 1—Body water compartments in a normal 70-kg man shown as percentage of body weight and in liters*

*Adapted from Edelman [3], p. 256.

At a finer level of detail, the compartments II through V are assumed for now to be osmotically equivalent,* by which is meant that the effective concentration of total solutes is identical, or that the chemical activity of H_2O as a species is identical, in the various compartments. The "concentration" of a species in the mathematical model is always expressed in the mole fraction scale.

Compartment I is an hypothetical compartment showing explicitly the partial pressures of gases in the venous blood. Since no gas phase actually exists, nitrogen is used to increase the sum of partial pressures to one atmosphere.

The viable system with nonzero metabolism is an <u>open</u> thermodynamic system. If it were <u>closed</u>, or <u>isolated</u>, the laws of conservation of mass, or of mass and energy, could be applied directly. However, mass and energy flow through the viable system, necessitating for the present mathematical model, the imposition of a rather restrictive condition in order to bring to bear the power of the conservation laws: namely, the condition that the system is at steady state. By the assumption of steady state, all flux rates for mass and energy through the system are

*See p. 59, and also Moore [2], and Robinson [6].

constant and there is a source of fuel for constant-rate metabolism. Then, on a per-unit-of-time basis, the conservation laws again apply.

Some of the complexity of viable systems can be very troublesome to analyze, and not only in the clinical laboratory. Viable systems can very easily lead to intractable mathematical formulations. At considerable convenience, it is assumed here that a range of steady-state conditions taken in the neighborhood of the standard resting state can be simulated without detailing the chemical reaction or diffusion rates, or the specific mechanisms of the active membranes. For example, the "rate" or "level of activity" of the sodium pump is taken to be constant throughout the viable range (which includes the standard dosages in the clinical laboratory); also, the mechanism of the sodium pump is not of interest here, only its net effect. Thus, processes which surely are rate-limited have been approximated in a reasonable manner; e.g., by incrementing the intrinsic free energy constants or electrochemical gradients, although these increments are not in the present model a function of mass inputs, mass distribution, or of temperature and pressure.

Finally, the modeled systems are not time dependent, sometimes a troublesome feature when attempting to relate results from the model with those from the clinical laboratory, especially for systems under stress. The mathematical model and computer program described here are not designed to trace the time transients induced in a living system by sudden stress, but only to simulate the new steady state that is the end result. This limitation is the reason for the nephrectomy, for example. The nephrectomized animal comes to a new steady state with regard to fluid balance after a period of 2-3 hours after an intravenous infusion. It is only the beginning and final states that we simulate here.

Within the limitation herein described, it is possible, however, to compute the normal distribution of the fluids and electrolytes in compartments I through V, including the effects of Gibbs-Donnan, sodium pump, constant flux, electrical and chemical gradients, differential solubilities, bicarbonate and hemoglobin buffering, and other chemical and electrochemical phenomena. Such detailed computation, though, involves millions of operations. Unless some method is available to cope with computations of this magnitude, a modeled system would be severely restricted and

highly approximate in order to bring it within the bounds of human comprehension and patience. It is proposed here to make such detailed computations a routine matter by using a computer and to present the results in a form which shows easily the relation of the parts to the whole, and the whole as a conceptual entity--i.e., as a detailed mathematical description of the fluid and electrolyte distribution. Further, it will be just as routine to add a chemical stress, or to test, say, a new chemical hypothesis relating to the system, each time computing the new steady state and comparing it with the standard in order to determine the model's predictive response to the stress or the possible validity of the hypothesis.

III. BACKGROUND OF THE MATHEMATICAL MODEL

The antecedents of the mathematical theory for this model are due to Gibbs [7], Dantzig, et al. [8], Clasen [9], and Shapiro and Shapley [10], taken chronologically. Work in the literature which develops from a view similar to the present research may be reviewed in McLean [11] who also mentions an earlier work by Borsook and Schott [12]. Dantzig [8] and DeHaven and DeLand [13] contain the detailed development of the earlier "respiratory" model, of which the present plasma and red cell compartments are elaborations; [8-10, 13] contain the details of the mathematical structure upon which these models are founded. Although the later elaborations described here are naturally more sophisticated than that of [8, 13], it will not be necessary to repeat here all the earlier rigorous arguments and justifications; e.g., the mathematical conditions for a unique solution, the effects of carbamino reactions and buffering on the dissociation curve for hemoglobin, or the important theorems on multiplicative systems. Instead, we wish to present a convincing argument that the thermodynamics and chemical phenomena which determine fluid and electrolyte balance are properly incorporated in the present

model. This will proceed from some basic chemical definitions.

For a species X_j in an ideal solution in a single phase or compartment, the partial mole free energy may be written (see Eq. (6), p. 20)

$$\left(\frac{\partial F}{\partial x_j}\right) = \Delta F_j^o + RT \ln \hat{x}_j \qquad (1)$$

where

ΔF_j^o = Free energy parameter of the j^{th} species;

x_j = Moles of the j^{th} species;

$\hat{x}_j$ = Mole fraction of the j^{th} species;

R = Gas constant;

T = Absolute temperature.

For the same substance in two compartments we may write

$$\left(\frac{\partial F}{\partial x_{jk}}\right) = \Delta F_{jk}^o + RT \ln \hat{x}_{jk}, \qquad k=1,2$$

where k designates the compartment name or number. If, now, the two compartments can communicate with each other via, say, a semi-permeable membrane or phase interface, we can speak of mole fraction gradients with respect to a substance across the membrane. In particular, a substance may have the same partial mole free energy in each compartment--viz.,

$$\left(\frac{\partial F}{\partial x_{j1}}\right) = \Delta F^{o}_{j1} + RT \ln \hat{x}_{j1}$$
$$= \left(\frac{\partial F}{\partial x_{j2}}\right) = \Delta F^{o}_{j2} + RT \ln \hat{x}_{j2} , \qquad (2)$$

but this does not imply equal mole fractions since the free energy parameters for the species X_{j1} may not be the same as for the species X_{j2}. Thus, we may have

$$\left(\frac{\Delta F^{o}_{j}}{RT}\right)_2 - \left(\frac{\Delta F^{o}_{j}}{RT}\right)_1 = \ln \frac{\hat{x}_{j1}}{\hat{x}_{j2}} \qquad (3)$$

where the left side, and hence the right side, is not zero.

If the chemical system is closed and Eq. (2) holds for every substance in the system and there are no intra-phase reactions, the system is said to be in equilibrium. For open systems, as most biological systems are, the

situation is much more complicated. An open system can never properly be said to be in equilibrium, but if it is in a steady state it may be approximated by appropriately defining additional restraints and by modifying the free energy parameters of an equilibrium model. An example of such a restraint is the sodium pump, an active transport process where work is done on a certain substance in a biological cell, creating a mole fraction gradient of the substance across a membrane. In such a case, we increment ΔF^{o}_{jk}, the free energy parameter, by an amount sufficient to provide the steady-state gradient. Here, ΔF^{o}, the standard free energy parameter, is the total work, except for the pressure volume work, done on or by the substance in bringing it to the present thermodynamic state. Usually, this quantity is not measurable in absolute terms, but can be computed or measured relative to some standard state. Generally speaking, we choose the state of the species in the plasma compartment to be the standard state.

In addition to mole fraction gradients which may derive from simple osmotic phenomena, biological cells usually have an electrical potential acting on the charged particles in and near the cell. An electrical potential will create an ion gradient across the membrane given by

$$\ell n \frac{\hat{x}_{j1}}{\hat{x}_{j2}} = \frac{z_j F^* E}{RT} \tag{4}$$

where z_j is the valence of the ion substance x_j, F^* is one Faraday, and E is the specific ion potential.

When both a chemical and an electrical potential are present, as in the Gibbs-Donnan phenomena, we have, for ideal solutions,

$$\ell n \frac{\hat{x}_{j1}}{\hat{x}_{j2}} = \frac{\left(\Delta F_{j2} - \Delta F_{j1}\right)}{RT} + \frac{z_j F^* E}{RT} = c_j \tag{5}$$

which determines the mole fraction ratio for the substance X_j across the membrane.

There may be other forces acting on the species of this system as well--e.g., pressure, temperature, but we assume here that pressure and temperature are uniform throughout the system. In order to make this assumption plausible, one need only consider the red cells floating in the plasma medium where it is unlikely that the disc-like red cell membrane would support an appreciable pressure gradient, even though the volume of the red cell may change ten or twenty per cent. In actuality, probably neither the

pressure nor the temperature are uniform throughout; for example, there are pressure gradients in capillaries, and the temperature of the interior of a cell may be higher than at the surface.

At this point, the interpretation of the right side of Eq. (5) is of considerable interest, because it details the difference between the energy states of the same substance on opposite sides of a membrane. The left side is the $\log_e$ of the corresponding ratio of mole fractions of the substance. Therefore, we have the opportunity to examine experiments in which, as a result of work being done on the species, changes result in the free energy states and, hence, in the mole fraction gradients for the substance between the compartments. Thus, for example:

a) Consider a system of two compartments separated by a semi-permeable membrane at equilibrium. Under osmotic forces only, but with zero hydrostatic pressure at equilibrium, the ratio of mole fractions across the membrane for each substance is one. The left side of Eq. (5) is zero and no work is required to move an infinitesimal amount of substance to either compartment; the right side is also zero.

b) The ratio of mole fractions is still one for the permeable species even if the membrane is impermeable to some uncharged species or even if the impermeable species have an equal electrical charge. However, under the conditions of unequally charged impermeable species, or hydrostatic forces, or a rigid membrane, then the Gibbs-Donnan relations appear. Under these conditions, work is done on the charged species and the right side of Eq. (5) is not zero.

c) Under the influence of electrostatic forces only, the left side will not in general be zero and the right side will yield the specific ion potential, as in Eq. (4).

d) Under the influence of an active membrane "pump" mechanism, we can regard the right side of Eq. (5) as the increment of net work done on each ion to cause a mole fraction gradient across the membrane.

Turning to the computer program, we wish to have a convenient format and theory for incorporating into the computations such thermodynamic phenomena as these listed immediately above, and at the same time to be able to compute the steady states of all pertinent inter- and intra-compartmental chemical reactions. We can make a statement on equilibrium for the computer, equivalent to that above, by stipulating that, in a dilute chemical milieu, a reversible equilibrium obtains when the Gibbs thermodynamic free energy function, $F(x)$, is minimized under the mass action and electrochemical restraints [14]. For steady states, the reactions will proceed until the available free energy is minimized under the functional restraints of the open system. The general restraints for an open thermodynamic steady-state system are the conservation of mass and energy on a per-unit-of-time basis. But particularly for biological systems, additional functional restraints occur in the form of mass action laws, osmotic forces, active membrane pumps, electrical potentials, and intraphase reactions.

We will assume that the free energy function to be minimized can be written

$$F(x) = \sum_{k} \sum_{j \epsilon k} x_j \left(\Delta F_j^o + RT \ln \hat{x}_j \right) , \quad k=1,\ldots,p \qquad (6)$$

and that the conservation of mass and conservation of charge restraints are of the form

$$\sum_{k} \sum_{j \epsilon k} a_{ij} x_j - b_i = E_i = 0 . \qquad \begin{matrix} i=1,\ldots,m \\ k=1,\ldots,p \end{matrix} \qquad (7)$$

where the a_{ij} are the stoichiometric chemical equation coefficients or, in the case of conservation of charge, the valence, and the b_i are the total moles of input of the i^{th} species. Of course, $x_j \geq 0$ for all j since the moles of a species must be positive or zero. See [10] for a rigorous discussion of Eq. (6) and its consequence, Eq. (1).

We may constrain the function explicitly by introducing arbitrary constants (the Lagrange multipliers), one for each conservation of mass or conservation of charge equation, thus defining

$$Q(x,\pi) = \frac{F(x)}{RT} - \sum_{i} \pi_i E_i \qquad (8)$$

where the π_i are arbitrary but will be determined uniquely, one for each restraint on the system. Now, the form $Q(x,\pi)$ is the restrained free energy function and at equilibrium we must have $dQ = 0$, just as for $F(x)$. Thus, we must have

$$\frac{\partial Q}{\partial x_j} = c_j + \ell n \hat{x}_j - \sum_i a_{ij}\pi_i = 0 , \quad \text{all } j$$

and (9)

$$\frac{\partial Q}{\partial \pi_i} = \sum_j a_{ij}x_j - b_i = 0 , \quad \text{all } i$$

where $c_j = (\Delta F_j^o/RT) + \ell nP$, the free energy parameter for each species; i.e., each partial derivative must be zero. On the computer, the first of Eqs. (9) will yield the inter- and intraphase electrochemical relations, such as (a) through (d) above, as well as the ordinary mass action equations; the second is, again, the conservation of mass.

The computer routine will find values of x_j, $\hat{x}_j$, and π_i, for all i and j, so that Eqs. (9) are satisfied for any arbitrary list of inter- and intraphase reactions; i.e., for an arbitrary chemical experiment with or without a membrane. The sequence of <u>human</u> events is to list all the

pertinent chemical reactions and species occurring in each compartment; assign to each species or reaction the appropriate ΔF_j^o, the free energy parameter which may be, for example, free energy of formation or reaction or membrane work function; and then to compute. The output will be the moles and mole fraction for each species in each compartment.

IV. THE MODEL OF THE COMPARTMENTED WHOLE BODY

Input and output data for the model of fluid and electrolyte distribution referred to in this discussion (called "Whole Body II") are shown in Tables I-V, appearing in this and the next section. These data will be used in the subsequent discussion to verify the statements of Sec. III; that is, to verify that all the mass action laws and electrochemical relations deemed appropriate and presently incorporated in the model are simultaneously satisfied by the computed distribution of species in the various compartments. These data will also be used to discuss the standard state distribution and some of the validation experiments showing the distributions after stress.

Table I, adapted from Edelman [3], is a standard distribution of body fluids and electrolytes for a 70-kg human male. Some of the data of Table I are difficult to determine in the laboratory--e.g., the distribution in the intracellular compartment--and some of the data are difficult to interpret--e.g., the proportion of the $SO_4^=$ ions bound or in solution--but this table will be accepted here as a reference standard since data from other sources (Moore [2], Spector [5]) generally concur in this

Table I

ELECTROLYTE COMPOSITION OF THE BODY FLUIDS*

ELECTROLYTES	SERUM (mEq/liter)	SERUM WATER (mEq/liter)	INTERSTITIAL FLUID[a] (mEq/liter)	INTRACELLULAR FLUID[b] (mEq/kg H_2O)
Cations:				
Sodium (Na^+)	142	152.7	145	10
Potassium (K^+)	4	4.3	4	160
Calcium (Ca^{++})	5	5.4	5	2
Magnesium (Mg^{++})	2	2.2	2	26
Total cations	153	164.6	156	198
Anions:				
Chloride (Cl^-)	101	108.5	114	3
Bicarbonate (HCO_3^-)	27	29.3	31	10
Phosphate ($HPO_4^=$)	2	2.2	2	100
Sulfate ($SO_4^=$)	1	1	1	20
Organic acids	6	6.4	7	
Protein	16	17.2	1	65
Total anions	153	164.6	156	198

[a]The average Gibbs-Donnan value of 0.95 is only approached by the univalent ions. These figures are, therefore, oversimplified and not completely accurate for Ca^{++}, Mg^{++}, $HPO_4^=$, and $SO_4^=$. In addition, no correction was made for the non-ionized fraction of Ca^{++} which does not gain access to the interstitial fluid.

[b]Average figures based largely on milliequivalents per kilogram of intracellular water of skeletal muscle.

*Adapted from Edelman [3].

distribution of species, often using Edelman as the original source.

It is necessary, however, to develop Table I in much more detail in order to use it as a standard for the present mathematical model. Table II, so developed from Table I and other sources [13], is a detailed breakdown of the distribution of substances in the standard state. For example, the "Intracellular" compartment of Table I has been divided into two compartments: "Red Cells" (taken together as a compartment and excluding the red cell membrane) and "Intracellular" (exclusive of the red cells). Table II will be used as a standard for comparison with the results of the mathematical model, which is even more detailed, to determine the accuracy of that model. In developing Table II, some empirical rules and generally accepted constants and factors were required (see also Fig. 1):

1.	Total Body Water	= 60% Total Body Mass (70 kg)	=	42.0 liters
2.	Total Intracellular Water	= 55% TBW	=	23.1 liters
3.	Plasma Volume	= 7.5% TBW	=	3.15 liters
4.	Red Cell Volume	(at 40% Total Body Hematocrit)	=	2.10 liters
5.	Red Cell Water	= 72.5% Red Cell Volume	=	1.52 liters
6.	Intracellular Water	= TICW - Red Cell Water	=	21.58 liters

7.	Plasma Water	= 94% Plasma Volume	=	2.96 liters
8.	Interstitial Water	= 20% Total Body Water	=	8.40 liters
9.	Specific Density of Water at 37°C		=	1.00669 ml/g
10.	55.19 moles H_2O at 37°C		=	1 liter
11.	Molecular Weight of Water		=	18.016
12.	RCW = (1.52/ 1.0067) x 1000	= 1509.8 g	=	83.303 moles
13.	PW = (2.96/ 1.0067) x 1000	= 2940.3 g	=	163.204 moles
14.	ISW = (8.40/ 1.0067) x 1000	= 8344.1 g	=	463.149 moles
15.	ICW = (21.58/ 1.0067) x 1000	= 21436.6 g	=	1189.83 moles
16.	pCO_2 at Venous Partial Pressure		=	45 mm
	pO_2 at Venous Partial Pressure		=	40 mm
17.	1 mole of Gas at 760 mm Hg at 37°C		=	25.44 liters

It is understood that the data of Table II are not definitive, and in some instances rather vague indeed. There are several cases where the data are merely the best approximations available instead of definite statements of laboratory fact. For example, the in vivo ratios of the protein-bound to the free small ions, especially for the double-valent ions of either sign, are not definitely known. Again, for the

Table II

EXPECTED DISTRIBUTIONS OF SPECIES FOR AVERAGE 70-Kg MAN

(mEq/liter except where otherwise specified)

SUBSTANCE	RED CELL	PLASMA	ISF	ICF	TOTAL
H_2O	83.3 M 1.52 lit	163.2 M 2.96 lit	463.1 M 8.40 lit	1189.8 M 21.58 lit	1899.40 M
Na^+	18.6	139.0	145.0	10.0	1920.19 mM
K^+	95.0	4.2	4.0	160.0	3698.50 mM
Ca^{++}		5.2	5.0	2.0	51.445 mM
Mg^{++}	5.1	1.7	2.0	26.0	296.96 mM
Cl^-	52.0	103.0	114.0	3.0	1449.39 mM
$SO_4^=$		1.0	1.0	20.0	222.22 mM
$HPO_4^=$		2.0	2.0	100.0	1092.30 mM
HCO_3^-	15.0	26.0	31.0	10.0	
Other Anions	10.0	5.0	7.0	0.3	101.9 mM
Protein	31.4[a] 25.29 mM/lit	16.0[a] 3.16 mM/lit	1.0[a] 4.0 mM/lit	53.0	1240.3 mM
Protein Avg. Chg.	-1.24	-5.06	-0.25	Undetermined	
Hb_4	5.05 mM/lit				10.605 mM
pH	7.19	7.39	7.40	6.80	
Volume	2.1 lit	3.15 lit	8.40 lit	21.58 lit	

[a]The average charge per mole of protein is fixed in this model. The average charge is computed empirically to give neutral electrical charge in each compartment, and considering the osmolarity of each compartment.

present model, the average charge of miscellaneous protein in the several compartments is computed considering the osmolarity, moles of protein, and neutral charge requirement rather than from average protein titration curves for each compartment, which are not available. Again, the empirical rules listed above may not be generally accepted (e.g., RCW = 72.5 per cent RCV), but in each case they represent the best compromise available at the present time.

With respect to such approximations, two paths for improvement are being pursued. First, using the computer model it is possible to test complex hypotheses of chemical behavior. An example of this approach is a sequence of tests now underway for small ion binding by protein. One such simple test can be described as follows: given an estimate of Ca^{++} bound by serum albumin [14], what is the average equilibrium constant for the intra-red cell protein Ca^{++} reaction which preserves the present (correct) hematocrit? That is, when Ca^{++} is experimentally bound to albumin but not to red cell protein, the hematocrit will shift (change in osmolarity), so it is a simple experiment to bind Ca^{++} to the red cell protein until the hematocrit is again correct. The resulting binding constant is an experimental average value for the red cell milieu at viable pH.

Secondly, there is obviously a good deal of information in the literature which has just not yet been incorporated, but should be. An example of such is the serum albumin titration curve [15]. The protein binding of serum albumin has been fairly well defined as regards the number and kind of sites at a particular pK. But this is precisely the kind of information required for this mathematical model, so it could be directly incorporated. Similarly, the phosphate buffering could be included when the amount of free phosphate has been determined. The hemoglobin buffering has been incorporated.

There are many relatively small problems of similar nature, each of which when defined will improve the accuracy of the model. At the present time, we are at pains to stress the model with relatively small stresses--one or two liters of solution--in order to test the qualitative performance and measure the quantitative accuracy against the literature and laboratory. It may be remarked here, but we will demonstrate in Sec. VI, that the model so far displays accuracy sufficient for clinical work and can apparently be improved to meet research requirements.

In Table II, the "Totals" column is the actual "input," the list of components, for the mathematical-computer model.

The essential problem for the mathematical program is then to redistribute these totals under mass action and electrochemical laws into the various compartments, reproducing Table II in more detail. We then have a basic, steady-state model, the details of which may be experimentally altered and verified.

Table III is a list of the 99 species and chemical reactions to be expected in the five "output" compartments:

I. A gas compartment containing gas which would be in equilibrium with plasma using nitrogen to increase the total pressure to one atmosphere;

II. The interiors, but not the membranes, of the red cells taken together as a compartment;

III. The plasma;

IV. The interstitial fluid;

V. The intracellular fluid.

This list labeled "Matrix" constitutes the complex description of the bio-physical system under study. It is probably a minimum list for an analytic study of the so-called "whole body" fluid balance; should other species or chemical reactions be determined to be pertinent or indispensable to the analytic description, they would simply be added to the matrix in the appropriate compartment. Examples of additions which are currently under consideration are phosphate and miscellaneous protein buffering, cation and anion binding

Table III

EXPECTED SPECIES AND INTRAPHASE REACTIONS

MATRIX: WHOLE BODY II 70 KG MALE GIL BRADHAM STANDARD

OUTPUT SPECIES	FREE ENERGY PARAMETER	INPUT SPECIES AND REACTIONS				
AIR COMPARTMENT						
O2	-10.940000	1.000 O2				
CO2	-7.690000	1.000 CO2				
N2	-11.520000	1.000 N2				
H2O	-36.600000	1.000 H+	1.000 OH-			
PLASMA COMPARTMENT						
O2	-0.	1.000 O2				
CO2	0.	1.000 CO2				
N2	0.	1.000 N2				
H+	0.	1.000 H+	-0.	-0.	1.000	*PLASM
OH-	0.	1.000 OH-	-0.	-0.	-1.000	*PLASM
CL-	0.	1.000 CL-	-0.	-0.	-1.000	*PLASM
NA+	0.	1.000 NA+	-0.	-0.	1.000	*PLASM
K+	0.	1.000 K+	-0.	-0.	1.000	*PLASM
CA++	0.	1.000 CA++	-0.	-0.	2.000	*PLASM
MG++	0.	1.000 MG++	-0.	-0.	2.000	*PLASM
SO4=	0.	1.000 SO4=	-0.	-0.	-2.000	*PLASM
HPO4=	0.	1.000 HPO4=	-0.	-0.	-2.000	*PLASM
UREA	0.	1.000 UREA				
GLUCOS	0.	1.000 GLUCOS				
LACTIC	0.	1.000 LACTIC	-0.	-0.	-1.000	*PLASM
HCO3-	-21.350000	-0.	1.000 OH-	1.000 CO2	-1.000	*PLASM
H2CO3	-32.840000	1.000 H+	1.000 OH-	1.000 CO2		
CO3=	6.260000	-1.000 H+	1.000 OH-	1.000 CO2	-2.000	*PLASM
H2O	-39.390000	1.000 H+	1.000 OH-			
PROTN	0.	1.000 MISCPL	-0.	-0.	-5.060	*PLASM
RED CELLS COMPARTMENT						
O2	-0.049000	1.000 O2				
CO2	0.	1.000 CO2				
N2	-0.500000	1.000 N2				
H+	0.	1.000 H+	-0.	-0.	1.000	*REDCE
OH-	0.	1.000 OH-	-0.	-0.	-1.000	*REDCE
CL-	0.	1.000 CL-	-0.	-0.	-1.000	*REDCE
NA+	2.157793	1.000 NA+	-0.	-0.	1.000	*REDCE
K+	-3.042507	1.000 K+	-0.	-0.	1.000	*REDCE
CA++	3.007158	1.000 CA++	-0.	-0.	2.000	*REDCE
MG++	-0.259000	1.000 MG++	-0.	-0.	2.000	*REDCE
SO4=	0.	1.000 SO4=	-0.	-0.	-2.000	*REDCE
HPO4=	0.	1.000 HPO4=	-0.	-0.	-2.000	*REDCE
UREA	0.	1.000 UREA				
GLUCOS	0.	1.000 GLUCOS				
LACTIC	0.	1.000 LACTIC	-0.	-0.	-1.000	*REDCE
HCO3-	-21.490000	-0.	1.000 OH-	1.000 CO2	-1.000	*REDCE
H2CO3	-32.840000	1.000 H+	1.000 OH-	1.000 CO2		
CO3=	6.120000	-1.000 H+	1.000 OH-	1.000 CO2	-2.000	*REDCE
H2O	-39.390000	1.000 H+	1.000 OH-			
PROTN	0.	1.000 MISCRE	-0.	-0.	-1.240	*REDCE
HB4	0.	-0.	1.000 HB4			
HB4O2	-12.842800	1.000 O2	1.000 HB4			
HB4O4	-24.768900	2.000 O2	1.000 HB4			
HB4O6	-36.182200	3.000 O2	1.000 HB4			
HB4O8	-51.245400	4.000 O2	1.000 HB4			
INTERSTITIAL COMPARTMENT						
O2	0.	1.000 O2				
CO2	0.	1.000 CO2				
N2	0.	1.000 N2				
H+	0.	1.000 H+	-0.	-0.	1.000	*EXCEL
OH-	0.	1.000 OH-	-0.	-0.	-1.000	*EXCEL
CL-	0.	1.000 CL-	-0.	-0.	-1.000	*EXCEL
NA+	-0.000074	1.000 NA+	-0.	-0.	1.000	*EXCEL
K+	0.020769	1.000 K+	-0.	-0.	1.000	*EXCEL
CA++	0.034480	1.000 CA++	-0.	-0.	2.000	*EXCEL
MG++	-0.006540	1.000 MG++	-0.	-0.	2.000	*EXCEL
SO4=	0.	1.000 SO4=	-0.	-0.	-2.000	*EXCEL
HPO4=	0.	1.000 HPO4=	-0.	-0.	-2.000	*EXCEL
UREA	0.	1.000 UREA				
GLUCOS	0.	1.000 GLUCOS				
LACTIC	0.	1.000 LACTIC	-0.	-0.	-1.000	*EXCEL
HCO3-	-21.350000	-0.	1.000 OH-	1.000 CO2	-1.000	*EXCEL
H2CO3	-32.840000	1.000 H+	1.000 OH-	1.000 CO2		
CO3=	6.260000	-1.000 H+	1.000 OH-	1.000 CO2	-2.000	*EXCEL
H2O	-39.390000	1.000 H+	1.000 OH-			
PROTN	0.	1.000 MISCEX	-0.	-0.	-0.250	*EXCEL
INTRACELL COMPARTMENT						
O2	-0.490000	1.000 O2				
CO2	0.	1.000 CO2				
N2	-0.500000	1.000 N2				
H+	2.000000	1.000 H+				
OH-	-2.000000	1.000 OH-				
CL-	0.	1.000 CL-				
NA+	6.011129	1.000 NA+				
K+	-0.331057	1.000 K+				
CA++	7.620247	1.000 CA++				
MG++	4.097990	1.000 MG++				
SO4=	-9.556927	1.000 SO4=				
HPO4=	-10.438020	1.000 HPO4=				
UREA	0.	1.000 UREA				
GLUCOS	0.	1.000 GLUCOS				
LACTIC	0.	1.000 LACTIC				
HCO3-	-23.490000	-0.	1.000 OH-	1.000 CO2		
H2CO3	-32.840000	1.000 H+	1.000 OH-	1.000 CO2		
CO3=	2.120000	-1.000 H+	1.000 OH-	1.000 CO2		
H2O	-39.390000	1.000 H+	1.000 OH-			
PROTN	0.	1.000 MISCIN				

by protein, and computable water-to-volume ratio for each compartment.

For each addition or alteration of the matrix, the output distribution of species, of course, changes, and we presume here that the solution space is feasible and continuous, and that the solution is uniquely a function of the total moles of input species and of the matrix [10]. To illustrate this statement, with all else the same, one may expect a continuously varying composition of the several compartments with a continuously varying input in the viable range (of, say, $NaHCO_3$); but also, the repeatability of identical experiments is independent of the previous history of the system, and identical results must be expected from identical inputs.

The first column of Table III is, then, the experimenter's best hypothesis as to the expected qualitative composition of each compartment. The second column is the relative free energy parameter, $(\Delta F_j^o/RT) = - \ln K_j$, for each species with respect to the plasma compartment, expressed as the natural log of K_j in mole fraction units [13]. This constant thus

has a variable interpretation: in the gas compartment it is the solubility coefficient for the gas species in plasma; for HCO_3^- in plasma, it is the reaction equilibrium constant for the formation of HCO_3^- (in this case from OH^- and CO_2); for the species Na^+ in red cells, it is proportional to the work function of the active membrane pump plus the specific ion potential; for Hb_4O_x in red cells, it is proportional to the Adair constants for oxygenation of hemoglobin; etc. The interpretation will depend upon the species opposite which it is found in Table III. We will discuss the meaning and use for these constants in some detail below.

The remaining columns of Table III list the specific input component of which the particular output species is composed; the starred entries are the valence of each species and are used for imposing a neutral charge requirement in each compartment.

Finally, Table IV is a computed distribution in moles, mole fractions, and moles per liter of water for each species in each compartment. The third scale, "moles per liter of water (in each compartment)," was chosen for convenience of computation. It may be converted to molal scale, "moles per Kg water," by multiplying by 1.0068.

Table IV

COMPUTER DISTRIBUTION OF FLUIDS AND ELECTROLYTES FOR STANDARD RESTING MAN

WHOLE BODY II 70 KG MALE GIL BRADHAM STANDARD

		AIR	PLASMA	RED CELLS	INTERSTITIAL	INTRACELL
X-BAR		1.00062E 03	1.62653E 02	8.36691E 01	4.65312E 02	1.20092E 03
PH		-0.	7.37875E 00	7.19610E 00	7.40021E 00	6.82157E 00
O2	MOLES	5.27412E 01	1.52041E-04	7.91931E-05	4.34955E-04	1.83239E-03
	MFRAC	5.27085E-02	9.34758E-07	9.81732E-07	9.34758E-07	1.52582E-06
	M/LH2O	0.	5.18889E-05	5.44948E-05	5.18889E-05	8.46990E-05
CO2	MOLES	6.09738E 01	4.53328E-03	2.24831E-03	1.29686E-02	3.34707E-02
	MFRAC	6.09361E-02	2.78708E-05	2.78708E-05	2.78708E-05	2.78708E-05
	M/LH2O	0.	1.54712E-03	1.54712E-03	1.54712E-03	1.54712E-03
N2	MOLES	8.25800E 02	1.33290E-03	1.08990E-03	3.81310E-03	1.62254E-02
	MFRAC	8.25289E-01	8.19471E-06	1.35108E-05	8.19471E-06	1.35108E-05
	M/LH2O	0.	4.54892E-04	7.49990E-04	4.54892E-04	7.49990E-04
H2O	MOLES	6.11045E 01	1.61714E 02	8.32034E 01	4.62626E 02	1.19399E 03
	MFRAC	6.10666E-02	9.94227E-01	9.94227E-01	9.94227E-01	9.94227E-01
	M/LH2O	0.	5.51900E 01	5.51900E 01	5.51900E 01	5.51900E 01
H+	MOLES	-0.	1.22498E-07	9.25181E-08	3.33544E-07	3.26262E-06
	MFRAC	-0.	7.53126E-10	1.14688E-09	7.16817E-10	2.71677E-09
	M/LH2O	-0.	4.18063E-08	6.36640E-08	3.97908E-08	1.50809E-07
OH-	MOLES	-0.	1.67889E-06	5.46782E-07	5.04618E-06	3.43628E-06
	MFRAC	-0.	1.03219E-08	6.77808E-09	1.08447E-08	2.86137E-09
	M/LH2O	-0.	5.72972E-07	3.76254E-07	6.01995E-07	1.58836E-07
CL-	MOLES	-0.	3.14514E-01	1.02431E-01	9.45325E-01	8.71201E-02
	MFRAC	-0.	1.93365E-03	1.26977E-03	2.03159E-03	7.25443E-05
	M/LH2O	-0.	1.07338E-01	7.04855E-02	1.12775E-01	4.02697E-03
NA+	MOLES	-0.	4.47309E-01	3.90469E-02	1.21804E 00	2.15791E-01
	MFRAC	-0.	2.75008E-03	4.84038E-04	2.61769E-03	1.79688E-04
	M/LH2O	-0.	1.52658E-01	2.68692E-02	1.45339E-01	9.97656E-03
K+	MOLES	-0.	1.26002E-02	1.99442E-01	3.36031E-02	3.49285E 00
	MFRAC	-0.	7.74664E-05	2.47235E-03	7.22161E-05	2.87517E-03
	M/LH2O	-0.	4.30020E-03	1.37241E-01	4.00875E-03	1.59602E-01
CA++	MOLES	-0.	8.38800E-03	4.76886E-04	2.10013E-02	2.15788E-02
	MFRAC	-0.	5.15698E-05	5.91163E-06	4.51338E-05	1.79685E-05
	M/LH2O	-0.	2.86266E-03	3.28157E-04	2.50540E-03	9.97440E-04
MG++	MOLES	-0.	3.22054E-03	4.79910E-03	8.40101E-03	2.80539E-01
	MFRAC	-0.	1.98000E-05	5.94911E-05	1.80546E-05	2.33603E-04
	M/LH2O	-0.	1.09911E-03	3.30238E-03	1.00222E-03	1.29674E-02
SO4=	MOLES	-0.	1.46834E-03	3.14028E-04	4.63691E-03	2.15801E-01
	MFRAC	-0.	9.02745E-06	3.89279E-06	9.96515E-06	1.79696E-04
	M/LH2O	-0.	5.01118E-04	2.16091E-04	5.53170E-04	9.97500E-03
HPO4=	MOLES	-0.	3.04189E-03	6.50555E-04	9.60602E-03	1.07900E 00
	MFRAC	-0.	1.87017E-05	8.06448E-06	2.06443E-05	8.98477E-04
	M/LH2O	-0.	1.03814E-03	4.47663E-04	1.14597E-03	4.98749E-02
UREA	MOLES	-0.	1.08015E-02	5.35708E-03	3.09005E-02	7.97510E-02
	MFRAC	-0.	6.64081E-05	6.64081E-05	6.64081E-05	6.64081E-05
	M/LH2O	-0.	3.68634E-03	3.68634E-03	3.68634E-03	3.68634E-03
GLUCOS	MOLES	-0.	1.26022E-02	6.25014E-03	3.60918E-02	9.30459E-02
	MFRAC	-0.	7.74787E-05	7.74787E-05	7.74787E-05	7.74787E-05
	M/LH2O	-0.	4.30088E-03	4.30088E-03	4.30088E-03	4.30088E-03
LACTIC	MOLES	-0.	2.13851E-02	6.98472E-03	6.42765E-02	5.92365E-03
	MFRAC	-0.	1.31477E-04	8.63369E-05	1.38136E-04	4.93259E-06
	M/LH2O	-0.	7.29833E-03	4.79260E-03	7.66801E-03	2.73810E-04
HCO3-	MOLES	-0.	8.75706E-02	3.28059E-02	2.63208E-01	2.06171E-01
	MFRAC	-0.	5.38388E-04	4.06673E-04	5.65659E-04	1.71677E-04
	M/LH2O	-0.	2.98862E-02	2.25746E-02	3.14000E-02	9.52987E-03
H2CO3	MOLES	-0.	6.44569E-06	3.19679E-06	1.84396E-05	4.75906E-05
	MFRAC	-0.	3.96284E-08	3.96284E-08	3.96284E-08	3.96284E-08
	M/LH2O	-0.	2.19979E-06	2.19979E-06	2.19979E-06	2.19979E-06
CO3=	MOLES	-0.	1.18746E-04	2.92121E-05	3.74991E-04	7.75005E-05
	MFRAC	-0.	7.30058E-07	3.62122E-07	8.05891E-07	6.45341E-08
	M/LH2O	-0.	4.05259E-05	2.01016E-05	4.47354E-05	3.58232E-06
PROTN	MOLES	-0.	9.96000E-03	5.31130E-02	3.36000E-02	1.14374E 00
	MFRAC	-0.	6.12346E-05	6.58368E-04	7.22096E-05	9.52385E-04
	M/LH2O	-0.	3.39916E-03	3.65463E-02	4.00839E-03	5.28673E-02
HB4	MOLES	-0.	-0.	9.15486E-04	-0.	-0.
	MFRAC	-0.	-0.	1.13487E-05	-0.	-0.
	M/LH2O	-0.	-0.	6.29969E-04	-0.	-0.
HB4O2	MOLES	-0.	-0.	1.55179E-03	-0.	-0.
	MFRAC	-0.	-0.	1.92365E-05	-0.	-0.
	M/LH2O	-0.	-0.	1.06783E-03	-0.	-0.
HB4O4	MOLES	-0.	-0.	1.05172E-03	-0.	-0.
	MFRAC	-0.	-0.	1.30374E-05	-0.	-0.
	M/LH2O	-0.	-0.	7.23713E-04	-0.	-0.
HB4O6	MOLES	-0.	-0.	4.26832E-04	-0.	-0.
	MFRAC	-0.	-0.	5.29114E-06	-0.	-0.
	M/LH2O	-0.	-0.	2.93714E-04	-0.	-0.
HB4O8	MOLES	-0.	-0.	6.66418E-03	-0.	-0.
	MFRAC	-0.	-0.	8.26112E-05	-0.	-0.
	M/LH2O	-0.	-0.	4.58579E-03	-0.	-0.

Given the input mole numbers, the free energy parameters, and the matrix, Table IV is the computed standard state distribution from the model which is to be compared with Table II. The computer program has been used to determine that unique distribution of species which satisfies the mass conservation equations and the inter- and intraphase mass action equations simultaneously; i.e., Eqs. (9). Thus, with the impermeable proteins in place in the appropriate compartments, and acting under the zero-charge constraints, the cation and anion pumps, the reaction equilibrium constants, differential solubilities, and other forcing functions, the system steady state is determined. From the result, various relations may be observed, as in the following section.

V. COMPUTED STANDARD STATE

A comparison of the expected standard values from Table II and the computed values from Table IV for all of the species of Table II is presented in Table V (on the same scale, mEq per liter).

Looking again now at Tables III and IV, we consider first the standard-state results before the addition of chemical stresses. It may be assumed that the computer program has satisfied Eqs. (9) for every output species, and every input row. We can read the list of chemical reactions and interphase reactions in Table III, compute the mass action relations from Eqs. (9), and compare the results to the printed output in Table IV. Several representative examples of this procedure follow.

UREA

Consider first an uncharged species, urea. It is assumed here that urea, after its production in the cell, does not undergo further chemical combination. Also, urea is uncharged and is not considered to be the subject of an active membrane pump mechanism. Consequently, the urea in solution should be at the same mole fraction in every compartment, as it is in Table IV. Looking at the second column in Table III, which is the list of relative

Table V

COMPARISON OF STANDARD VALUES AGAINST COMPUTED VALUES*

(mEq/liter except as otherwise noted)

	RED CELL	PLASMA	ISF	ICF
Na^+	18.6	139.0	145.0	10.0
	18.6	142.0	145.0	10.0
K^+	95.0	4.2	4.0	160.0
	95.0	4.0	4.0	160.0
Ca^{++}		5.2	5.0	2.0
	0.45	5.3	5.0	2.0
Mg^{++}	5.1	1.7	2.0	26.0
	4.6	2.0	2.0	26.0
Cl^-	52.0	103.0	114.0	3.0
	48.8	99.8	112.5	4.0
$SO_4^=$		1.0	1.0	20.0
	0.3	0.9	1.1	20.0
$HPO_4^=$		2.0	2.0	100.0
	0.65	1.9	2.3	100.0
HCO_3^-	15.0	26.0	31.0	10.0
	15.6	27.8	31.3	9.55
H_2O	83.3 M	163.2 M	463.1 M	1189.8 M
	80.2	161.7	462.6	1194.0
pH	7.19	7.39		
	7.20	7.38	7.40	6.82

*Standard value, taken from Table II, is shown above each computed value, taken from Table IV.

free energy values for each product species, it should be noted that the free energy value, $\Delta F^{o}_{urea}/RT$, is 0.0 for urea in each compartment. Then, from Eq. (3)--as well as Eqs. (9)--the urea mole fractions should be the same, and they are.

CO_2

Consider next the CO_2. Just as for the urea, the dissolved CO_2 has the same mole fraction in each of the fluid compartments. But in the gas compartment the CO_2 concentration is 0.0609 moles/mole, or 6.09 per cent, or 46 mm of mercury. This is slightly higher than the alveolar sac concentration of 5.26 per cent or 40 mm. A gas compartment appears because we have used excess nitrogen to raise the total gas pressure to one atmosphere. This introduces a slight error in the nitrogen content of the entire system, but the error is negligible. We note, too, that this gas phase acts as a slight buffer for the whole system--the response to chemical stress will be slightly distorted, but the error from this source is thought to be slight, relative to other approximations.

In Table III, the second line, it may be seen that the value of $\Delta F^{o}_{CO_2}/RT = -7.69$, which is the $\log_e K$ on the mole fraction scale where K is proportional to the solubility

coefficient. From the sixth line in Table III, as well as lines 31, 51, and 71, all of which are CO_2 in compartments II through V, the $\Delta F_j^o/RT = 0.0$. Using subscript 2 for the input component CO_2, and lines 2 and 6 from Table III as an illustration of the application of Eqs. (9), we have

$$-7.69 + \ell n \left[CO_{2\ gas} \right] - 1.0\ \pi_2 = 0$$

$$0.0 + \ell n \left[CO_{2\ plasma} \right] - 1.0\ \pi_2 = 0$$

or, subtracting,

$$\ell n\ \frac{\left[CO_{2\ gas} \right]}{\left[CO_{2\ plasma} \right]} = 7.69$$

so that the concentration ratio of CO_2 gas to plasma dissolved is antilog$_e$ 7.69 which, of course, it turns out to be in Table IV. Similar equations work out for the other gases except that there is slight difference in solubility between intra- and extracellular milieu. For example, for O_2 plasma vs. O_2 red cells, we have

$$-0.49 + \ell n\ \hat{x}_5 - \pi_1 = 0$$

$$0.0 + \ell n\ \hat{x}_{30} - \pi_1 = 0$$

$$\ell n \left(\hat{x}_5 / \hat{x}_{30} \right) = 0.49$$

$$\ell n \frac{\left[{}^{O}_{2 \text{ red cells}} \right]}{\left[{}^{O}_{2 \text{ plasma}} \right]} = 0.49 \ . \tag{10}$$

We will always take the plasma value of $\Delta F^{O}/RT$ for each species as the relative standard state, setting it to 0.0.

$\underline{Cl^-}$

Consider next the Cl^- ion, a charged species but not actively pumped by a membrane mechanism. Between red cells and plasma, using Eqs. (9), we have for Cl^-,

$$0.0 + \ell n \, \hat{x}_{10} - \pi_6 + \pi_{22} = 0$$

$$0.0 + \ell n \, \hat{x}_{35} - \pi_6 + \pi_{21} = 0$$

or, subtracting,

$$x_{10}/x_{35} = \exp \left(\pi_{21} - \pi_{22} \right) \ . \tag{11}$$

Now, restraints 21 and 22 are the chemical thermodynamic zero-charge requirements on the plasma and red cell compartments, respectively. This results in an electrochemical

potential for each charged species, the specific ion potential, using Eqs. (4), and can be evaluated. From Table IV,

$$\ell n \frac{\hat{x}_{10}}{\hat{x}_{35}} = \ell n \frac{1.270}{1.934} = \frac{ZF^{*}E}{RT} = \pi_{21} - \pi_{22}$$

or,

$$E = - \frac{1.987 \times 310}{23062} \ell n\ 1.523 = -11.2 \text{ millivolts} \quad (12)$$

which potential, the so-called Donnan potential, should be applicable, with the proper sign, to every charged species as well as to Cl^- between red cell and plasma. In addition, however, some of the species are actively pumped and some have a different valence. Those with double valence, $SO_4^{=}$ for example, have the same specific ion potential but their concentration ratio is the square of the chloride ratio as a result of the double valence.

The chloride ratio is often taken as a measure of the Gibbs-Donnan effect resulting from the impermeable proteins and charge restraints. In this case, the concentration ratio from red cells to plasma is 1.52:1, whereas the ratio of Cl^- concentration from plasma to interstitial fluid is

$\hat{x}_{35}/\hat{x}_{55} = 0.952$, and from plasma to intracellular fluid is 26.25:1.

GIBBS-DONNAN EFFECT

The Gibbs-Donnan effect, a fundamental electrochemical effect in biological systems with membranes, requires special mention. This effect is manifest when there exists a steady ion concentration gradient across a semipermeable membrane owing to the presence of impermeable charged species plus a zero electrostatic charge requirement in each compartment, as is the case in each compartment and across each membrane of the present model. In deference to this model, we will further limit this discussion to those systems where H_2O is a permeable species, where the membrane will not support an appreciable hydrostatic pressure gradient; i.e., it is movable. In the physiological range, the red cells-plasma system exhibits these properties, and we assume them for this report with respect to the plasma-interstitial interface and the interstitial-intracellular interface.

Speaking qualitatively, we first note that the ionization constant for H_2O is identical in each compartment; i.e., $\ell n\ K_w = 39.39$ mole-fraction scale or $\log K_w = -13.6163$ moles/liter scale at 37^oC. That is, we assume that the

activity of water is the same in each compartment and thus we show the mole fraction of H_2O to be identical, as computed in Table IV. Conversely, the concentration of total solutes is the same, which we interpret to mean that the osmolarity of each compartment is the same.

Now, under these conditions, if the protein were uncharged and the Na^+ pump absent, the volumes of the compartments would be proportional to the protein content in moles in each compartment and all species would be uniformly distributed. The same would hold if all protein had the same charge, say, univalent [13]. But suppose, first, that the proteins in the various compartments have varying average charges (as those in Table III which were computed from Table II in order to make each compartment neutral). Under the neutral charge restraint, the distribution of the small permeable ions is no longer uniform, since a different amount of base is bound per unit of protein in each compartment. Thus, under the equal osmolarity restraint, the distribution of volumes of compartments is not simply proportional to the protein alone, but to the protein plus the ions restrained by the neutral charge restraint. Permeable H_2O also shifts through the membranes until all species, including the permeable components,

attain the required concentration ratios, the Gibbs-Donnan ratios. In this idealized system, these ratios are 1 for uncharged species and are given by the specific ion potential for charged species.

Finally, if we also now apply the Na^+ pump, forcing specific ions to assume new gradients, the permeable ions and volumes of compartments again shift to satisfy the new requirements as well. Again in this idealized system, the compartment volume ratios now--in fact, always--satisfy the following arithmetic, using red cell-plasma relations as an example:

$$\frac{(\text{molality of all permeable solutes})_{\text{plasma}}}{(\text{molality of all permeable solutes})_{\text{red cell}}} = 1$$

$$= \frac{(\text{molality of uncharged permeable species})_{\text{plasma}}}{(\text{molality of uncharged permeable species})_{\text{red cell}}}$$

or

$$\frac{(\text{solutes in moles})_{\text{plasma}}}{(\text{solutes in moles})_{\text{red cell}}} = \frac{(\text{moles of } H_2O)_{\text{plasma}}}{(\text{moles of } H_2O)_{\text{red cell}}}$$

$$= \frac{(\text{fixed protein + restrained ions in moles})_{\text{plasma}}}{(\text{fixed protein + restrained ions in moles})_{\text{red cell}}}$$

$\underline{Na^+}$

The Na^+ ion is an example of an ion which not only responds to the Gibbs-Donnan effect since it is charged, but is also actively pumped by or at the membrane. We can compute the increments necessary for the standard free energy parameter to yield the appropriate gradient, which will be proportional to the minimum free energy requirements of the active membrane pump, as follows: Since the effect of Gibbs-Donnan is to drive negative ions out of the red cell, positive ions will be driven into the red cell by the Gibbs-Donnan effect, against the Na^+ pump. Therefore, the plasma-to-red-cell-sodium ratio, whatever it is found to be, must be increased by the Gibbs-Donnan effect to give the total free energy requirements by the Na^+ pump.

More precisely, if h is the sodium ratio, then h is the result of a chemical potential (the active transport process) plus an electrical potential (the Gibbs-Donnan potential) as in Eq. (5), or

$$\ln h = K_{Na+} + E \times z_{Na+}$$

$$h = e^{(K_{Na+})(E\ z_{Na+})}$$

where z_{Na^+} is the valence of Na^+, E is the specific ion (membrane) potential (with sign) and K_{Na^+} is a measure of the activity of the sodium pump. Equation (4) is a method for computing E, while K_{Na^+} must be obtained from the gross activity of the Na^+ pump; i.e., the ratio of mole fractions which would result from the pump alone.

Thus, from Table IV, which compares well with the <u>in vivo</u> values of Table II, the apparent Na^+ mole fraction ratio gives

$$\ell n \frac{\left[Na^+_{plasma}\right]}{\left[Na^+_{red\ cells}\right]} = 1.7373 \ .$$

Now, from Eq. (3)

$$\Delta F = RT\ \ell n \frac{\hat{x}_{36}}{\hat{x}_{11}} = 1.987 \times 310 \times 1.7373$$

$$= 1070 \text{ cal/mole of } Na^+ \qquad (13)$$

at the steady-state level of the standard man. But, this apparent gradient must be increased by the Cl^- gradient to get the minimum net free energy requirements of the pump. Thus,

$$\ell n \frac{\left[Na^{+}_{plasma}\right]}{\left[Na^{+}_{red\ cell}\right]} + \ell n \frac{\left[Cl^{-}_{plasma}\right]}{\left[Cl^{-}_{red\ cell}\right]} = 1.7373 + 0.4205 = 2.1578$$

and

$$\Delta F = RT \times 2.1578 = 1329 \text{ cal/mole of } Na^{+}$$

at steady state [16].

It must be noted that it is not accurate to regard these energy quantities as the "work" of the Na^{+} pump, since in an open, in vivo system the total work is also a function of viscosity, permeability, and other factors. But in a corresponding idealized system without "frictional losses" the work expended would be 1329 cal/mole Na^{+} by the corresponding Na^{+} pump in order to maintain the apparent Na^{+} gradient. Neither, it should be noted, is this the free energy required to bring the system from classical equilibrium to this steady state, but only that required to maintain the system at the apparent level as measured by the fixed Na^{+} gradient.

This brings into relief the true role of the number 2.1578 which is purely empirical on our part as the level

of the active pump required to give the proper Na^+ gradient, a measure of the gross activity of the active transport mechanism. Of course, it can be computed as well from standard physiological tables with the proper conversion to mole fraction scale. The Ca^{++} gradient constant is computed much the same as for Na^+, while K^+ and Mg^{++} have work functions of opposite sign and are aided by the Gibbs-Donnan effect. It should be noted that the constants given here as a measure of the gross pump activity may be appreciably altered when better estimates are available for the binding of small cations (especially divalent) intracellularly. For example, if one-half of the available Mg^{++} were bound intracellularly [17], but none interstitially, the ratio of free Mg^{++} would be reduced by two and the apparent work of the active pump by $\ell n 2$.

THE BLOOD COMPARTMENTS

The plasma and red cells compartments which make up the blood of the mathematical model have been described in detail in [13]. The compositions and interrelations of these two compartments, as well as the macroscopic and microscopic validation of the blood model, was a separate problem preliminary to the present description of the so-called "whole body." Consequently, we will note here some

of the characteristics of these compartments from the computed Table IV, but without detailed justification.

The pH of plasma is 7.38, and of red cells is 7.19, about 0.2 pH points apart. Both compartments are slightly acid since we are simulating venous blood. Venous blood is presumed to be in steady-state equilibrium with the body tissues, the intracellular compartment. It has a whole body hematocrit of 40 per cent, 5 per cent lower than venous blood at the heart. The hemoglobin is 74.4 per cent saturated at a venous pO_2 of 40 mm, pCO_2 of 46 mm; the corresponding point on the curves from the data of Dill [18] is 72 per cent saturated. The venous pO_2 of 40 mm is assumed in the vicinity of active body cells, but it is an arbitrary value, an input to the model; if we input 100 mm of O_2 and 40 mm of CO_2, the blood would change to arterial and the whole body system would shift to that which would be in equilibrium with arterial blood at the exit of the lung. The pO_2 of 40 mm was determined to be the average, whole-body venous oxygen pressure, not including the pulmonary region.

The Na^+ mole fraction ratio is 5.7:1 plasma to red cell and the K^+ ratio is 32:1 in the opposite direction at the standard steady state. The double-valent ions' concentration ratios, both positive and negative, have been

determined to satisfy corresponding values from the literature but the meaning of these ratios in the literature is not yet perfectly clear since the interaction and binding of these ions to protein has not been completely spelled out, and is not represented in this model.

The bicarbonate system is, of course, present, as well as a reasonable approximation to the buffering power of hemoglobin. The carbamino reactions of hemoglobin are also included, though not explicitly shown in Table IV. Other pertinent details are given in [13].

THE INTERSTITIAL FLUID COMPARTMENT

The interstitial fluid is generally regarded as an ultrafiltrate of plasma, with, however, a "normal" small complement of proteins which perhaps derive from a "leakage" through the vessel walls. As such, it apparently has no outstanding properties or functions with regard to electrolyte distribution, but merely forms a chemical and physical buffering environment for the cells. With regard to the electrolyte distribution, though, this present work indicates that there may be small cation pumps between the plasma and interstitial fluid. This is indicated by the fact that the cation gradients reported in Table II cannot be accounted

for by the simple Gibbs-Donnan effect alone. Thus, a measure of the Gibbs-Donnan effect is the ratio of concentrations of Cl^- which is 0.95 across the vessel walls, while for, say, K^+, the ratio is 0.93. This small discrepancy, indicating work performed by an active ion transport across the vessel walls, is small, and could very well be accounted for by slight inconsistency or variation in the reported data, or possibly by specific cation binding by proteins, which will be discussed later. However, Sawyer [19] cited some evidence for a similar conclusion from some experiments in vitro, but his theoretical explanation is complicated by factors not considered here--e.g., electrophoresis at or in the membrane. Manery [20] reports similar small discrepancies.

There is another interesting and important, although from another point of view perhaps obvious, relationship of the interstitial fluid to the whole body model which is pointed up by regarding the interstitial fluid as an environment for the cells. This environment is defined in terms of concentrations of species, and the relationships of the various species across the membrane are also expressed in terms of concentrations (Eqs. (3) and (9)). That is, in a steady-state problem, if the volume of the interstitial fluid were

instantaneously 100 times larger with exactly the same composition, no change would occur in the concentration of the species in the interior of the cells since the concentration ratios remain the same. Similarly, in the mathematical model, if the interstitial volume with the same composition is halved or reduced to zero, no change will occur in the plasma or in the cells. Obviously, the same statement holds for any other compartment as well.*

But, it is in the validation of the model under chemical stress that the volumes of the model compartments are critical in determining the response of the model, since the amount of a species sequestered or transported in a changing system is a function of the volume through which a given mass of the species is distributed. This says that one may construct a steady-state mathematical model of a biochemical system with arbitrary compartment volumes, but that during the validation of the model the volumes must be proportional to those of the experimental animal in order to expect a similar response.

THE INTRACELLULAR COMPARTMENT

The intracellular compartment is composed of the interiors of the body cell mass, not including red cells, with

*See Isotonic Contraction, Section VI.

particular reference to those cells which quickly exchange fluids and electrolytes with the environment, as contrasted to cells found in tendon and dermis. On the average, this compartment may be regarded as muscle tissue. The intracellular compartment is an even more complex matter than the red cells. In addition to strong cation pumps across the cellular membranes, an apparent active H^+ ion pump is also present as well as apparent anion pumps--"apparent" because the actual mechanisms for maintaining the rather unusual gradients for some of these ions are not clear at this time.* Some examples of this complicated situation follow.

For a point of comparison, the red cell acidity in relation to plasma can be explained by a simple Gibbs-Donnan gradient mechanism. But, the simple Gibbs-Donnan gradient for H^+ into the intracellular compartment would drive those cells very acid indeed. The Gibbs-Donnan concentration gradient for monovalent ions between interstitial and intracellular compartments is approximately 28:1, which would have to be satisfied by H^+ ions as well,† implying a pH of about 5.5 intracellularly. In order to bring this

*See Conway [17].

†See Van Slyke, et al. [21].

up to an accepted level, say 6.8, a fairly active H^+ pump is required, driving H^+ ion out of the cell. The minimum free energy expended for this apparent H^+ pump would be on the order of 2500 cal/mole of H^+ at steady state. This number is obtained using the mathematical model, Table III, intracellular compartment. It is empirically derived by experiment with the model as the work required to maintain pH 6.8 inside the body cells.

This fundamental derivation of the energy required can be said to be dependent upon the accepted analyses of free chloride ion. If the free chloride Donnan concentration ratio is really on the order of 28:1, outside to inside muscle cells, and we assume the membrane inactive with respect to chloride, then the H^+ ion concentration ratio would be 1:28 without an H^+ pump. Alternatives to an H^+ pump suggest themselves: a) the interior of <u>in vivo</u> cells is pH 5.5; b) the intracellular chloride analysis is in error; c) there is an active chloride pump, which could explain a great deal but seems to serve no purpose and would inhibit CO_2 transport; d) there is a very great difference in H_2O activity intracellularly--which goes against the assumption of uniform osmolarity; e) the intracellular milieu is undoubtedly very complex and apparent anomaly in the H^+ ion concentration ratio may be just one manifestation of that

fact. This simulation is obviously not equipped with either the detail or the sophistication to model that complexity. Again, we model the function and not the mechanism, if we supply an H^+ pump.

The large Cl^- gradient also implies a strong Na^+ pump in order to maintain the reported Na^+ gradient against the Gibbs-Donnan forces--and almost no K^+ pump. The Na^+ pump can be computed from

$$\frac{\left[Na^+_{extra}\right]}{\left[Na^+_{intra}\right]} = \frac{2.618 \times 10^{-3}}{1.797 \times 10^{-4}} = 14.57 \qquad (14)$$

which is the apparent or net mole fraction gradient. But this pump must work against the Gibbs-Donnan gradient,

$$\frac{\left[Cl^-_{extra}\right]}{\left[Cl^-_{intra}\right]} = \frac{2.03 \times 10^{-3}}{7.25 \times 10^{-5}} = 28.00$$

or,

$$\Delta F = RT \times \ell n(28 \times 14.57) = 3642 \text{ cal/mole of } Na^+ \qquad (15)$$

at steady state.

The K^+ pump, correspondingly, is only

$$\Delta F = RT \times 0.331 = 200 \text{ cal/mole} \qquad (16)$$

since it is aided by the Gibbs-Donnan potential.

Ca^{++} and Mg^{++} have apparent pump values which may be computed similarly to the K^+ and Na^+. In the cases of Ca^{++} and Mg^{++}, it is not yet clear how much effect protein binding will have in the apparent gradients--nor actually for Na^+ and K^+ [18]. Certainly some double-valent cations--as well as anions [15]--are bound *in vivo*, although the reported quantitative chemical analyses from which Table II is composed do not indicate the qualitative or quantitative structure of the complex binding in the milieu. In fact, there are very few quantitative studies bearing on the cation binding *in vivo*, although there is a literature on cation or base binding by proteins in various contexts--e.g., protein structure theory, competitive binding with protons, and multiple equilibria, and blood buffering (see, for example, Tanford [22, especially Chapter 8]. Loken, *et al.* [14], report that some 50 per cent of the total calcium in serum may be bound to serum albumin with a pK = 2.18 at pH = 7.35. Also, Gurd and Goodman [23] report a pK = 2.8 for Zn^{++} with

serum albumin, but generally these numbers are difficult to come by in the literature.

It may not be much in error to consider that the single-valent ions are completely ionized, but it is fairly well agreed that the double-valent ions are significantly bound and in complex ways; e.g., to the membrane. We have, nevertheless, not incorporated such binding into the model and for the reason that, at best, the quantitative aspects are undecided; also, we make the assumption that the binding inside the cells is in about the same proportion to that outside, so that the ratio of concentration of free ions, those affected by Gibbs-Donnan, would be about the same as in the present model. This assumption has no foundation, but the alternatives are still controversial and the implications very involved [6]. For example, the possibilities of specific binding of H_2O to protein and an active water pump may be required to explain the resulting osmotic disequilibrium. Alternatively, one may have to consider osmotic coefficients for proteins or hydration of small ions.

On the other hand, neither have we shown the double-valent anions tied up as compounds, which they surely are.

The organic phosphates and sulfates are, by definition, bound and perhaps most of the inorganic phosphate and sulfate as reported in [5] are bound in some way, principally to the double-valent cations [24]. Apparently, only 15 per cent of the inorganic phosphate is protein-bound [25], and the same may be true for sulfate. The double-valent metallic salts are not highly ionized at this temperature and may also claim some of the anions.

The result is that, in dealing with the double-valent anions as though they were all free, very strong active membrane pumps are required to keep the $SO_4^{=}$ and $HPO_4^{=}$ in the cell in the quantities reported. If the free $SO_4^{=}$ and $HPO_4^{=}$ in the cell were reduced by binding, the free gradients would be decreased and the pump values correspondingly reduced. The present $SO_4^{=}$ pump, as an example, requires $\Delta F^{o} = RT \times 9.55 = 5882$ cal/mole to maintain steady state. It is interesting to conjecture that the binding energy of $SO_4^{=}$ in the protein must be at least this great or else the sulfate ions would move out into the extracellular spaces.

The quantities involved are not small, being on the same order as Na^{+} and HCO_3^{-}. Thus, tying up the double-valent anions will affect the osmolarity as well as the Gibbs-Donnan associated phenomena.

Without further laboratory and mathematical experiments, it is too early to consider all the ramifications of the double-valent ions, but it is a point demanding attention.

H_2O

Finally, let us consider the species H_2O. Since we assume, for now, uniform hydrostatic pressure and uniform activity for H_2O in each compartment, and since it is uncharged, the water distribution will be a function of the gross osmolarity. Thus, as Van Slyke [21] points out, the water distribution will be determined so that the ratio

$$\frac{\text{molecules + ions of solute}}{\text{molecules of water}}$$

is identical in each compartment. This is a widely held assumption for biological systems, but it may be naive. Robinson [6], in an excellent review of intracellular water metabolism, discusses the possibility that the body cells are not in osmotic equilibrium and finally concludes that the consensus of opinion is that they are. The contrary could imply the active transport of H_2O by some means--say, an active membrane pump--the result of which is a mole fraction gradient for the species H_2O across the cell membrane.

An alternative explanation for such an H_2O gradient was advanced by Spanner [26] and discussed more recently by DeHaven [29]. If it is assumed that the interior of the muscle cells operates at a slightly elevated temperature because of the metabolic activity, even one-fourth or one-half degree is sufficient to appreciably alter the H_2O activity. Further, this theory can be incorporated so that the cell will appear to have an H^+ (or alternately an OH^-) pump as required relative to the other compartments, even though the basic cause is a change in H_2O activity. The hydration shells of protein can also effectively bind the polarized H_2O molecules, thus changing the activity coefficient. As much as 16 per cent of the water in human red cells may be bound to hemoglobin [6] and this, combined with the binding of double-valent ions, makes for a complex osmotic and Donnan problem. None of these sorts of hypotheses have yet been incorporated except experimentally. Further work is obviously required.

Almost 63 per cent of the total 1898 moles of water in the compartments considered here appears in the intracellular spaces, excluding red cells; about 25 per cent appears in the interstitial space; and only 13 per cent, or 4.4 liters, in the blood.

VI. VALIDATION OF THE MODEL

INTRODUCTION

The process of testing the mathematical model of fluid and electrolyte balance consists of two parts: first, verifying that the reference standard state has been simulated within a reasonable tolerance; and second, performing biochemical stress experiments that cause a deviation from the standard state, similar to experiments performed in the laboratory. A wide range of experiments will generally be required to test a new model, and modifications will be made on the basis of the results of these experiments.

A model of the standard viable state is not necessarily unique. For example, it may be possible to obtain in a second model the same mathematical distribution of species (within, say, 1 per cent) as the reference model by trading off, say, an active membrane pump against the protein binding of a species plus a slight change in the amount or average charge of protein. But while the distribution of species of these two models may be almost identical at the standard state, they generally will stress quite differently--i.e., the validity of a model must be measured by its correct response to a wide variety of stresses.

Validation experiments deal first with qualitative aspects--(Does the distribution of species shift--in detail--in the proper direction under stress?), and secondly with quantitative aspects--(Do the results compare numerically with the laboratory results?). As the experiments proceed, discrepancies between the model and laboratory results give rise to improvements in the model and improvements in laboratory practice.

Improvements in the model might include, for example, a re-examination of the buffering system, or the addition of a new chemical species or reaction, or the inclusion of new facts on, say, glucose gradients. Improvements in laboratory practice have included greater attention to preparation and detail, re-examination of conditions and assumptions and their implications (e.g., eliminating the use of fluoride compounds in experimental live blood), and determining new requirements and techniques in the experimental method.

Generally speaking, the experimental data available on body electrolyte distribution under stress are either not sufficiently detailed or are not sufficiently controlled to be useful for validation of the model. Much of the data comes from the human clinics where certain controls and

measurements are impossible. But, also, the absence from the model of certain clinical hypotheses--e.g., glucose permeability--limits the choice of usable data. Most of the experiments we discuss here have been chosen from the literature for their distinct qualitative characteristics--i.e., abnormalities in distribution which were well recognized and documented--in order to illustrate the similarities, the differences, and the detail of the mathematical model. However, three of the validation experiments, involving 22 dogs, which we discuss were carefully designed to produce in the laboratory the detailed data required for validation of the model under controlled conditions.

The use of dogs in the laboratory is an approximation felt to be acceptable at this stage of validation. The reported chemical similarities of dog and man [28] enhance our expectation of qualitative similarities in response to stress. In detail, of course, the responses will be different, and for certain experiments the dog response may even be misleading.

Table VI, the normal human electrolyte distribution from the computer, is a repeat of Table IV, included for reference in this more convenient location. The figures shown, together with the subsequent discussion, summarize

Table VI

COMPUTER DISTRIBUTION OF FLUIDS AND ELECTROLYTES FOR STANDARD RESTING MAN

WHOLE BODY II 70 KG MALE GIL BRADHAM STANDARD

		AIR	PLASMA	RED CELLS	INTERSTITIAL	INTRACELL
X-BAR		1.00062E 03	1.62653E 02	8.36691E 01	4.65312E 02	1.20092E 03
PH		-0.	7.37875E 00	7.19610E 00	7.40021E 00	6.82157E 00
O2	MOLES	5.27412E 01	1.52041E-04	7.91931E-05	4.34955E-04	1.83239E-03
	MFRAC	5.27085E-02	9.34758E-07	9.81702E-07	9.34758E-07	1.52582E-06
	M/LH2O	0.	5.18889E-05	5.44948E-05	5.18889E-05	8.46990E-05
CO2	MOLES	6.09738E 01	4.53328E-03	2.24831E-03	1.29686E-02	3.34707E-02
	MFRAC	6.09361E-02	2.78708E-05	2.78708E-05	2.78708E-05	2.78708E-05
	M/LH2O	0.	1.54712E-03	1.54712E-03	1.54712E-03	1.54712E-03
N2	MOLES	8.25800E 02	1.33290E-03	1.08990E-03	3.81310E-03	1.62254E-02
	MFRAC	8.25289E-01	8.19471E-06	1.35108E-05	8.19471E-06	1.35108E-05
	M/LH2O	0.	4.54892E-04	7.49990E-04	4.54892E-04	7.49990E-04
H2O	MOLES	6.11045E 01	1.61714E 02	8.32034E 01	4.62626E 02	1.19399E 03
	MFRAC	6.10666E-02	9.94227E-01	9.94227E-01	9.94227E-01	9.94227E-01
	M/LH2O	0.	5.51900E 01	5.51900E 01	5.51900E 01	5.51900E 01
H+	MOLES	-0.	1.22498E-07	9.25181E-08	3.33544E-07	3.26262E-06
	MFRAC	-0.	7.53126E-10	1.14688E-09	7.16817E-10	2.71677E-09
	M/LH2O	-0.	4.18063E-08	6.36640E-08	3.97908E-08	1.50809E-07
OH-	MOLES	-0.	1.67889E-06	5.46782E-07	5.04618E-06	3.43628E-06
	MFRAC	-0.	1.03219E-08	6.77808E-09	1.08447E-08	2.86137E-09
	M/LH2O	-0.	5.72972E-07	3.76254E-07	6.01995E-07	1.58836E-07
CL-	MOLES	-0.	3.14514E-01	1.02431E-01	9.45325E-01	8.71201E-02
	MFRAC	-0.	1.93365E-03	1.26977E-03	2.03159E-03	7.25443E-05
	M/LH2O	-0.	1.07338E-01	7.04855E-02	1.12775E-01	4.02697E-03
NA+	MOLES	-0.	4.47309E-01	3.90469E-02	1.21804E 00	2.15791E-01
	MFRAC	-0.	2.75008E-03	4.84038E-04	2.61769E-03	1.79688E-04
	M/LH2O	-0.	1.52658E-01	2.68692E-02	1.45309E-01	9.97456E-03
K+	MOLES	-0.	1.26002E-02	1.99442E-01	3.36031E-02	3.45285E 00
	MFRAC	-0.	7.74664E-05	2.47235E-03	7.22161E-05	2.87517E-03
	M/LH2O	-0.	4.30020E-03	1.37241E-01	4.00875E-03	1.59602E-01
CA++	MOLES	-0.	8.38800E-03	4.76886E-04	2.10013E-02	2.15788E-02
	MFRAC	-0.	5.15698E-05	5.91163E-06	4.51338E-05	1.79685E-05
	M/LH2O	-0.	2.86266E-03	3.28157E-04	2.50540E-03	9.97440E-04
MG++	MOLES	-0.	3.22054E-03	4.79910E-03	8.40101E-03	2.80539E-01
	MFRAC	-0.	1.98000E-05	5.94911E-05	1.80546E-05	2.33603E-04
	M/LH2O	-0.	1.09911E-03	3.30238E-03	1.00222E-03	1.29674E-02
SO4=	MOLES	-0.	1.46834E-03	3.14028E-04	4.63691E-03	2.15801E-01
	MFRAC	-0.	9.02745E-06	3.89279E-06	9.96515E-06	1.79696E-04
	M/LH2O	-0.	5.01118E-04	2.16091E-04	5.53170E-04	9.97500E-03
HPO4=	MOLES	-0.	3.04189E-03	6.50555E-04	9.60602E-03	1.07900E 00
	MFRAC	-0.	1.87017E-05	8.06448E-06	2.06443E-05	8.98477E-04
	M/LH2O	-0.	1.03814E-03	4.47663E-04	1.14597E-03	4.98749E-02
UREA	MOLES	-0.	1.08015E-02	5.35708E-03	3.09005E-02	7.97510E-02
	MFRAC	-0.	6.64081E-05	6.64081E-05	6.64081E-05	6.64081E-05
	M/LH2O	-0.	3.68634E-03	3.68634E-03	3.68634E-03	3.68634E-03
GLUCOS	MOLES	-0.	1.26022E-02	6.25014E-03	3.60518E-02	9.30459E-02
	MFRAC	-0.	7.74787E-05	7.74787E-05	7.74787E-05	7.74787E-05
	M/LH2O	-0.	4.30088E-03	4.30088E-03	4.30088E-03	4.30088E-03
LACTIC	MOLES	-0.	2.13851E-02	6.96472E-03	6.42765E-02	5.92365E-03
	MFRAC	-0.	1.31477E-04	8.63369E-05	1.38136E-04	4.93259E-06
	M/LH2O	-0.	7.29833E-03	4.79260E-03	7.66801E-03	2.73810E-04
HCO3-	MOLES	-0.	8.75706E-02	3.28059E-02	2.63238E-01	2.06171E-01
	MFRAC	-0.	5.38388E-04	4.06673E-04	5.65659E-04	1.71677E-04
	M/LH2O	-0.	2.98862E-02	2.25746E-02	3.14000E-02	9.52987E-03
H2CO3	MOLES	-0.	6.44569E-06	3.19679E-06	1.84396E-05	4.75906E-05
	MFRAC	-0.	3.96284E-08	3.96284E-08	3.96284E-08	3.96284E-08
	M/LH2O	-0.	2.19979E-06	2.19979E-06	2.19979E-06	2.19979E-06
CO3=	MOLES	-0.	1.18746E-04	2.92121E-05	3.74991E-04	7.75005E-05
	MFRAC	-0.	7.30058E-07	3.62122E-07	8.05891E-07	6.45341E-08
	M/LH2O	-0.	4.05259E-05	2.01016E-05	4.47354E-05	3.58232E-06
PROTN	MOLES	-0.	9.96000E-03	5.31100E-02	3.36000E-02	1.14374E 00
	MFRAC	-0.	6.12346E-05	6.58368E-04	7.22096E-05	9.52385E-04
	M/LH2O	-0.	3.39916E-03	3.65463E-02	4.00839E-03	5.28673E-02
HB4	MOLES	-0.	-0.	9.15486E-04	-0.	-0.
	MFRAC	-0.	-0.	1.13487E-05	-0.	-0.
	M/LH2O	-0.	-0.	6.29969E-04	-0.	-0.
HB4O2	MOLES	-0.	-0.	1.55179E-03	-0.	-0.
	MFRAC	-0.	-0.	1.92365E-05	-0.	-0.
	M/LH2O	-0.	-0.	1.06783E-03	-0.	-0.
HB4O4	MOLES	-0.	-0.	1.05172E-03	-0.	-0.
	MFRAC	-0.	-0.	1.30374E-05	-0.	-0.
	M/LH2O	-0.	-0.	7.23713E-04	-0.	-0.
HB4O6	MOLES	-0.	-0.	4.26832E-04	-0.	-0.
	MFRAC	-0.	-0.	5.29114E-06	-0.	-0.
	M/LH2O	-0.	-0.	2.93714E-04	-0.	-0.
HB4O8	MOLES	-0.	-0.	6.66418E-03	-0.	-0.
	MFRAC	-0.	-0.	8.26112E-05	-0.	-0.
	M/LH2O	-0.	-0.	4.58579E-03	-0.	-0.

pertinent data taken from the accompanying detailed tables of computed distribution from the computer.

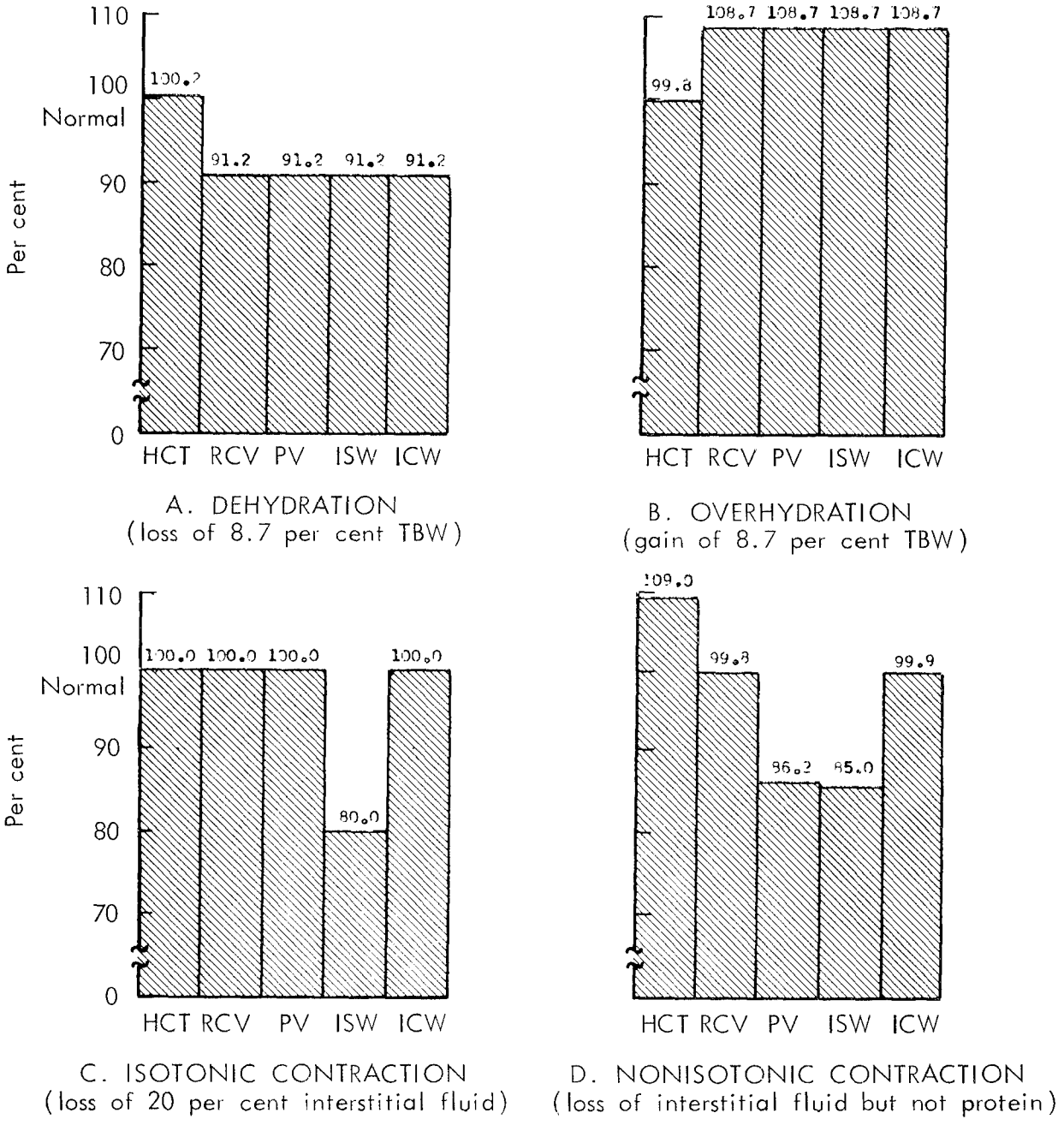
The first three experiments to be discussed are general results verifying the conclusions of Bland [28, Chap. 8]. Then follow experiments by Bradham [1] on nephrectomized dogs, and, finally, various experiments from other sources.

DEHYDRATION--HYPERTONIC CONTRACTION

Hypertonic contraction is the loss of water, or dehydration, with little or no corresponding loss of salt [28]. Bland notes that water loss is shared by the extra- and intracellular compartments. In fact, if the H_2O activity is the same in all compartments, the water loss in all compartments will be proportional, as shown in Fig. 2A and in Table VII.

The hematocrit in the model, however, is very slightly increased (0.2 per cent), although the osmolarity of both plasma and red cells increases equally. The hematocrit change is due to a Gibbs-Donnan movement of electrolytes caused by a slight difference in the fixed, charged protein in the two compartments.

Na^+ mole fraction is increased, but preferentially intracellularly. This change in Na^+ gradient may partially



HCT = Hematocrit RCV = Red cell volume ICW = Intracellular water
PV = Plasma volume ISW = Interstitial water (exclusive of red cells)

Fig. 2—Contraction and expansion experiments (computed)

Table VII

HYPERTONIC CONTRACTION

TABLE VII LOSS OF THREE LITERS OF BODY WATER (FIG. 2A)

		AIR	PLASMA	RED CELLS	INTERSTITIAL	INTRACELL
X-BAR		1.00059E 03	1.48522E 02	7.39394E 01	4.24909E 02	1.09665E 03
PH		-0.	7.41671E 00	7.23190E 00	7.43818E 00	6.85098E 00
O2	MOLES	5.27405E 01	1.38834E-04	7.25875E-05	3.97193E-04	1.67331E-03
	MFRAC	5.27093E-02	9.34772E-07	9.81716E-07	9.34772E-07	1.52584E-06
	M/LH2O	0.	5.19180E-05	5.45253E-05	5.19180E-05	8.47465E-05
CO2	MOLES	6.09797E 01	4.13994E-03	2.36101E-03	1.18440E-02	3.05682E-02
	MFRAC	6.09436E-02	2.78743E-05	2.78743E-05	2.78743E-05	2.78743E-05
	M/LH2O	0.	1.54816E-03	1.54816E-03	1.54816E-03	1.54816E-03
N2	MOLES	8.25802E 02	1.21713E-03	9.99010E-04	3.48211E-03	1.48170E-02
	MFRAC	8.25314E-01	8.19496E-06	1.35112E-05	8.19496E-06	1.35112E-05
	M/LH2O	0.	4.55154E-04	7.50423E-04	4.55154E-04	7.50423E-04
H2O	MOLES	6.10694E 01	1.47584E 02	7.34724E 01	4.22225E 02	1.08972E 03
	MFRAC	6.10333E-02	9.93684E-01	9.93684E-01	9.93684E-01	9.93684E-01
	M/LH2O	0.	5.51900E 01	5.51900E 01	5.51900E 01	5.51900E 01
H+	MOLES	-0.	1.02437E-07	7.80464E-08	2.78928E-07	2.73191E-06
	MFRAC	-0.	6.89710E-10	1.05555E-09	6.56443E-10	2.49115E-09
	M/LH2O	-0.	3.83070E-08	5.86258E-08	3.64593E-08	1.38360E-07
OH-	MOLES	-0.	1.67307E-06	5.44237E-07	5.02907E-06	3.42023E-06
	MFRAC	-0.	1.12648E-08	7.36058E-09	1.18356E-08	3.11881E-09
	M/LH2O	-0.	6.25655E-07	4.08812E-07	6.57361E-07	1.73221E-07
CL-	MOLES	-0.	3.14547E-01	1.02320E-01	9.45498E-01	8.70241E-02
	MFRAC	-0.	2.11785E-03	1.38384E-03	2.22518E-03	7.93540E-05
	M/LH2O	-0.	1.17627E-01	7.68594E-02	1.23588E-01	4.40743E-03
NA+	MOLES	-0.	4.47154E-01	3.93764E-02	1.21766E 00	2.16001E-01
	MFRAC	-0.	3.01070E-03	5.32550E-04	2.86569E-03	1.96965E-04
	M/LH2O	-0.	1.67217E-01	2.95782E-02	1.59163E-01	1.09396E-02
K+	MOLES	-0.	1.25787E-02	2.00852E-01	3.35469E-02	3.45152E 00
	MFRAC	-0.	8.46926E-05	2.71644E-03	7.89508E-05	3.14735E-03
	M/LH2O	-0.	4.70389E-03	1.50873E-01	4.38499E-03	1.74806E-01
CA++	MOLES	-0.	8.37781E-03	4.82887E-04	2.09760E-02	2.16083E-02
	MFRAC	-0.	5.64079E-05	6.53085E-06	4.93659E-05	1.97040E-05
	M/LH2O	-0.	3.13294E-03	3.62729E-04	2.74182E-03	1.09438E-03
MG++	MOLES	-0.	3.21197E-03	4.85245E-04	8.37873E-03	2.80517E-01
	MFRAC	-0.	2.16263E-05	6.56274E-05	1.97189E-05	2.55795E-04
	M/LH2O	-0.	1.20114E-03	3.64500E-03	1.09520E-03	1.62071E-02
SO4=	MOLES	-0.	1.47189E-03	3.12851E-04	4.64855E-03	2.15787E-01
	MFRAC	-0.	9.91023E-06	4.23118E-06	1.09401E-05	1.96770E-04
	M/LH2O	-0.	5.50422E-04	2.35003E-04	6.07623E-04	1.09287E-02
HPO4=	MOLES	-0.	3.04934E-03	6.48141E-04	9.63052E-03	1.07897E 00
	MFRAC	-0.	2.05312E-05	8.76586E-06	2.26649E-05	9.83884E-04
	M/LH2O	-0.	1.14032E-03	4.86862E-04	1.25883E-03	5.46657E-02
UREA	MOLES	-0.	1.07992E-02	5.37625E-03	3.08957E-02	7.97388E-02
	MFRAC	-0.	7.27115E-05	7.27115E-05	7.27115E-05	7.27115E-05
	M/LH2O	-0.	4.03845E-03	4.03845E-03	4.03845E-03	4.03845E-03
GLUCOS	MOLES	-0.	1.25995E-02	6.27250E-03	3.60463E-02	9.30317E-02
	MFRAC	-0.	8.48330E-05	8.48330E-05	8.48330E-05	8.48330E-05
	M/LH2O	-0.	4.71169E-03	4.71169E-03	4.71169E-03	4.71169E-03
LACTIC	MOLES	-0.	2.13874E-02	6.95716E-03	6.42883E-02	5.91712E-03
	MFRAC	-0.	1.44002E-04	9.40928E-05	1.51299E-04	5.39566E-06
	M/LH2O	-0.	7.99796E-03	5.22599E-03	8.40328E-03	2.99679E-04
HCO3-	MOLES	-0.	8.72778E-02	3.26573E-02	2.62348E-01	2.05233E-01
	MFRAC	-0.	5.87643E-04	4.41676E-04	6.17423E-04	1.87146E-04
	M/LH2O	-0.	3.26381E-02	2.45310E-02	3.42922E-02	1.03942E-02
H2CO3	MOLES	-0.	5.88320E-06	2.92886E-06	1.68313E-05	4.34400E-05
	MFRAC	-0.	3.96117E-08	3.96117E-08	3.96117E-08	3.96117E-08
	M/LH2O	-0.	2.20006E-06	2.20006E-06	2.20006E-06	2.20006E-06
CO3=	MOLES	-0.	1.29231E-04	3.15960E-05	4.08142E-04	8.41349E-05
	MFRAC	-0.	8.70115E-07	4.27323E-07	9.60565E-07	7.67203E-08
	M/LH2O	-0.	4.83269E-05	2.37339E-05	5.33491E-05	4.26110E-06
PROTN	MOLES	-0.	9.96000E-03	5.31100E-02	3.36000E-02	1.16376E 00
	MFRAC	-0.	6.70608E-05	7.18291E-04	7.90758E-05	1.04294E-03
	M/LH2O	-0.	3.72461E-03	3.98944E-02	4.39193E-03	5.79259E-02
HB4	MOLES	-0.	-0.	8.03844E-04	-0.	-0.
	MFRAC	-0.	-0.	1.08717E-05	-0.	-0.
	M/LH2O	-0.	-0.	6.03821E-04	-0.	-0.
HB4O2	MOLES	-0.	-0.	1.42248E-03	-0.	-0.
	MFRAC	-0.	-0.	1.92384E-05	-0.	-0.
	M/LH2O	-0.	-0.	1.06852E-03	-0.	-0.
HB4O4	MOLES	-0.	-0.	1.00647E-03	-0.	-0.
	MFRAC	-0.	-0.	1.36121E-05	-0.	-0.
	M/LH2O	-0.	-0.	7.56028E-04	-0.	-0.
HB4O6	MOLES	-0.	-0.	4.26434E-04	-0.	-0.
	MFRAC	-0.	-0.	5.76734E-06	-0.	-0.
	M/LH2O	-0.	-0.	3.20323E-04	-0.	-0.
HB4O8	MOLES	-0.	-0.	6.95077E-03	-0.	-0.
	MFRAC	-0.	-0.	9.40063E-05	-0.	-0.
	M/LH2O	-0.	-0.	5.22118E-03	-0.	-0.

account for the reported slight loss of Na^+ in dehydration [28]; i.e., it may also sequester intracellularly.

OVERHYDRATION--HYPOTONIC EXPANSION

Hypotonic expansion occurs when the system is stressed with added water alone [28]. In this case, Fig. 2B and Table VIII, the results are opposite to hypertonic contraction, as might be expected. Water is distributed proportionately to all compartments, diluting all compartments uniformly. These results, it must be remembered, are the initial responses of the body prior to initiation of compensatory mechanisms and kidney action.

In the model, there is a very slight shift of electrolytes, but general edema, of course, occurs. The results of both this and the previous dehydration experiment are conditioned by the assumption of equal osmolarity in all compartments, which is expressed here by requiring that H_2O as a species have the same activity in all compartments. Had we not made this assumption of uniform H_2O activity, the various compartments would change volume in proportion to the H_2O activity during a water stress.

The pH of the system changes uniformly with water addition. With overhydration, the pH decreases and with dehydration, the pH rises compared to the standard. The

Table VIII

OVERHYDRATION--HYPOTONIC EXPANSION

TABLE VIII GAIN OF THREE LITERS OF BODY WATER (FIG. 28)

		AIR	PLASMA	RED CELLS	INTERSTITIAL	INTRACELL
X-BAR		1.00064E 03	1.76781E 02	8.73741E 01	5.05724E 02	1.30522E 03
PH		-0.	7.34394E 00	7.16330E 00	7.36539E 00	6.78726E 00
O2	MOLES	5.27619E 01	1.65246E-04	8.57766E-05	4.72726E-04	1.99152E-03
	MFRAC	5.27081E-02	9.34751E-07	9.81694E-07	9.34751E-07	1.52581E-06
	M/LH2O	0.	5.18646E-05	5.44693E-05	5.18646E-05	8.46595E-05
CO2	MOLES	6.09680E 01	4.92646E-03	2.43490E-03	1.40933E-02	3.83734E-02
	MFRAC	6.09289E-02	2.78675E-05	2.78675E-05	2.78675E-05	2.78675E-05
	M/LH2O	0.	1.54623E-03	1.54623E-03	1.54623E-03	1.54623E-03
N2	MOLES	8.25798E 02	1.44866E-03	1.18046E-03	4.14416E-03	1.76342E-02
	MFRAC	8.25268E-01	8.19451E-06	1.35105E-05	8.19451E-06	1.35105E-05
	M/LH2O	0.	4.54672E-04	7.49628E-04	4.54672E-04	7.49628E-04
H2O	MOLES	6.11339E 01	1.75841E 02	8.69096E 01	5.03035E 02	1.29829E 03
	MFRAC	6.10946E-02	9.94683E-01	9.94683E-01	9.94683E-01	9.94683E-01
	M/LH2O	0.	5.51900E 01	5.51900E 01	5.51900E 01	5.51900E 01
H+	MOLES	-0.	1.44316E-07	1.08119E-07	3.92953E-07	3.83925E-06
	MFRAC	-0.	8.16353E-10	1.23742E-09	7.77011E-10	2.96145E-09
	M/LH2O	-0.	4.52994E-08	6.86583E-08	4.31125E-08	1.63206E-07
OH-	MOLES	-0.	1.68416E-06	5.49150E-07	5.06188E-06	3.45103E-06
	MFRAC	-0.	9.52680E-09	6.28504E-09	1.00092E-08	2.64402E-09
	M/LH2O	-0.	5.28995E-07	3.48725E-07	5.55359E-07	1.46703E-07
CL-	MOLES	-0.	3.14472E-01	1.02539E-01	9.45171E-01	8.72085E-02
	MFRAC	-0.	1.77888E-03	1.17356E-03	1.86895E-03	6.68149E-05
	M/LH2O	-0.	9.87009E-02	6.51151E-02	1.03698E-01	3.70723E-03
NA+	MOLES	-0.	4.47438E-01	3.87637E-02	1.21841E 00	2.15603E-01
	MFRAC	-0.	2.53103E-03	4.43424E-04	2.40923E-03	1.65184E-04
	M/LH2O	-0.	1.40434E-01	2.46034E-02	1.33676E-01	9.16526E-03
K+	MOLES	-0.	1.26193E-02	1.98137E-01	3.36545E-02	3.45409E 00
	MFRAC	-0.	7.13839E-05	2.26769E-03	6.65471E-05	2.64636E-03
	M/LH2O	-0.	3.96073E-03	1.25823E-01	3.69237E-03	1.46833E-01
CA++	MOLES	-0.	8.39704E-03	4.71367E-04	2.10246E-02	2.15520E-02
	MFRAC	-0.	4.74996E-05	5.39481E-06	4.15732E-05	1.65121E-05
	M/LH2O	-0.	2.63551E-03	2.99331E-04	2.30669E-03	9.16175E-04
MG++	MOLES	-0.	3.22825E-03	4.74980E-03	8.42138E-03	2.80561E-01
	MFRAC	-0.	1.82613E-05	5.43616E-05	1.66521E-05	2.14952E-04
	M/LH2O	-0.	1.01323E-03	3.01625E-03	9.23943E-04	1.19266E-02
SO4=	MOLES	-0.	1.46505E-03	3.15153E-04	4.62629E-03	2.15814E-01
	MFRAC	-0.	8.28738E-06	3.60694E-06	9.14785E-06	1.65346E-04
	M/LH2O	-0.	4.59825E-04	2.00131E-04	5.07569E-04	9.17422E-03
HPO4=	MOLES	-0.	3.03496E-03	6.52862E-04	9.58370E-03	1.07903E 00
	MFRAC	-0.	1.71679E-05	7.47204E-06	1.89504E-05	8.26700E-04
	M/LH2O	-0.	9.52562E-04	4.14586E-04	1.05147E-03	4.58694E-02
UREA	MOLES	-0.	1.08031E-02	5.33945E-03	3.09049E-02	7.97625E-02
	MFRAC	-0.	6.11102E-05	6.11102E-05	6.11102E-05	6.11102E-05
	M/LH2O	-0.	3.39070E-03	3.39070E-03	3.39070E-03	3.39070E-03
GLUCOS	MOLES	-0.	1.26041E-02	6.22957E-03	3.60569E-02	9.30594E-02
	MFRAC	-0.	7.12976E-05	7.12976E-05	7.12976E-05	7.12976E-05
	M/LH2O	-0.	3.95595E-03	3.95595E-03	3.95595E-03	3.95595E-03
LACTIC	MOLES	-0.	2.13822E-02	6.97205E-03	6.42661E-02	5.92966E-03
	MFRAC	-0.	1.20953E-04	7.97954E-05	1.27077E-04	4.54302E-06
	M/LH2O	-0.	6.71108E-03	4.42745E-03	7.05088E-03	2.52070E-04
HCO3-	MOLES	-0.	8.78353E-02	3.29441E-02	2.63996E-01	2.07031E-01
	MFRAC	-0.	4.96859E-04	3.77047E-04	5.22016E-04	1.58617E-04
	M/LH2O	-0.	2.75682E-02	2.09204E-02	2.89641E-02	8.80089E-03
H2CO3	MOLES	-0.	7.00795E-06	3.46368E-06	2.00479E-05	5.17416E-05
	MFRAC	-0.	3.96419E-08	3.96419E-08	3.96419E-08	3.96419E-08
	M/LH2O	-0.	2.19953E-06	2.19953E-06	2.19953E-06	2.19953E-06
CO3=	MOLES	-0.	1.09880E-04	2.71888E-05	3.46976E-04	7.18794E-05
	MFRAC	-0.	6.21562E-07	3.11177E-07	6.86038E-07	5.50705E-08
	M/LH2O	-0.	3.44874E-05	1.72656E-05	3.80682E-05	3.05559E-06
PROTN	MOLES	-0.	9.96000E-03	5.31100E-02	3.36000E-02	1.14376E 00
	MFRAC	-0.	5.63408E-05	6.07846E-06	6.64396E-05	8.76278E-04
	M/LH2O	-0.	3.12607E-03	3.37263E-02	3.68639E-03	4.86203E-02
HB4	MOLES	-0.	-0.	1.03365E-03	-0.	-0.
	MFRAC	-0.	-0.	1.18301E-05	-0.	-0.
	M/LH2O	-0.	-0.	6.56394E-04	-0.	-0.
HB4O2	MOLES	-0.	-0.	1.68106E-03	-0.	-0.
	MFRAC	-0.	-0.	1.92398E-05	-0.	-0.
	M/LH2O	-0.	-0.	1.06752E-03	-0.	-0.
HB4O4	MOLES	-0.	-0.	1.09314E-03	-0.	-0.
	MFRAC	-0.	-0.	1.25110E-05	-0.	-0.
	M/LH2O	-0.	-0.	6.94175E-04	-0.	-0.
HB4O6	MOLES	-0.	-0.	4.25661E-04	-0.	-0.
	MFRAC	-0.	-0.	4.87170E-06	-0.	-0.
	M/LH2O	-0.	-0.	2.70306E-04	-0.	-0.
HB4O8	MOLES	-0.	-0.	6.37649E-03	-0.	-0.
	MFRAC	-0.	-0.	7.29792E-05	-0.	-0.
	M/LH2O	-0.	-0.	4.04925E-03	-0.	-0.

mechanism for this is not entirely clear, but may be accounted for in part by the carbonic acid content. With added water, more CO_2 is dissolved, forming bicarbonate and hydrogen ions in relation to the fixed protein and base in the system. In any case, the mass action equations in the buffering system shift the concentration of products of ionization with changing concentrations, so the pH shift may be subtly related to the total buffering.

ISOTONIC CONTRACTION AND EXPANSION

Isotonic expansion or contraction occurs as a result of the gain or loss of extracellular fluid [28]; e.g., infusion of interstitial fluid or intravenous infusion of plasma, or the loss of either one. Bland [28] points out that in such a case the concentration gradients have not changed and one can predict that the electrolytes will not move, nor will the solute. Therefore, only that compartment which has been altered will change in volume, and will represent the only change. Of course, if the plasma volume alone changes, so does the hematocrit, but a change in interstitial volume will not affect the hematocrit (Fig. 2C and Table IX). Also, note, we are discussing the idealized case, before the body compensatory mechanisms or the kidney come into play.

Table IX

ISOTONIC EXPANSION AND CONTRACTION

TABLE IX LOSS OF INTERSTITIAL FLUID WITH PROTEIN (FIG. 2C)

		AIR	PLASMA	RED CELLS	INTERSTITIAL	INTRACELL
X-BAR		1.00062E 03	1.62648E 02	8.06678E 01	3.72254E 02	1.20092E 03
PH		-0.	7.37874E 00	7.19609E 00	7.40020E 00	6.82156E 00
O2	MOLES	5.27412E 01	1.52037E-04	7.91917E-05	3.47967E-04	1.83239E-03
	MFRAC	5.27085E-02	9.34758E-07	9.81702E-07	9.34758E-07	1.52582E-06
	M/LH2O	0.	5.18888E-05	5.44947E-05	5.18888E-05	8.46990E-05
CO2	MOLES	6.09738E 01	4.53314E-03	2.24828E-03	1.03750E-02	3.34707E-02
	MFRAC	6.09361E-02	2.78708E-05	2.78708E-05	2.78708E-05	2.78708E-05
	M/LH2O	0.	1.54712E-03	1.54712E-03	1.54712E-03	1.54712E-03
N2	MOLES	8.25800E 02	1.33286E-03	1.08989E-03	3.05051E-03	1.62254E-02
	MFRAC	8.25289E-01	8.19471E-06	1.35108E-05	8.19471E-06	1.35108E-05
	M/LH2O	0.	4.54892E-04	7.49990E-04	4.54892E-04	7.49990E-04
H2O	MOLES	6.11049E 01	1.61709E 02	8.02021E 01	3.70104E 02	1.19399E 03
	MFRAC	6.10667E-02	9.94227E-01	9.94227E-01	9.94227E-01	9.94227E-01
	M/LH2O	0.	5.51900E 01	5.51900E 01	5.51900E 01	5.51900E 01
H+	MOLES	-0.	1.22496E-07	9.25181E-08	2.66840E-07	3.26268E-06
	MFRAC	-0.	7.53135E-10	1.14690E-09	7.16025E-10	2.71681E-09
	M/LH2O	-0.	4.18069E-08	6.36651E-08	3.97913E-08	1.50811E-07
OH-	MOLES	-0.	1.67881E-06	5.46763E-07	4.03693E-06	3.43623E-06
	MFRAC	-0.	1.03217E-08	6.77796E-09	1.08446E-08	2.86132E-09
	M/LH2O	-0.	5.72964E-07	3.76248E-07	6.01988E-07	1.58833E-07
CL-	MOLES	-0.	3.14504E-01	1.02429E-01	7.56268E-01	8.71198E-02
	MFRAC	-0.	1.93364E-03	1.26976E-03	2.03159E-03	7.25440E-05
	M/LH2O	-0.	1.07337E-01	7.56852E-02	1.12775E-01	4.02695E-03
NA+	MOLES	-0.	4.47296E-01	3.90464E-02	9.74442E-01	2.15792E-01
	MFRAC	-0.	2.75008E-03	4.84040E-04	2.61768E-03	1.79688E-04
	M/LH2O	-0.	1.52658E-01	2.68693E-02	1.45339E-01	9.97459E-03
K+	MOLES	-0.	1.25998E-02	1.99439E-01	2.68826E-02	3.45286E 00
	MFRAC	-0.	7.74662E-05	2.47235E-03	7.22158E-05	2.87517E-03
	M/LH2O	-0.	4.30018E-03	1.37241E-01	4.00873E-03	1.59602E-01
CA++	MOLES	-0.	8.38774E-03	4.76881E-04	1.68011E-02	2.15789E-02
	MFRAC	-0.	5.15697E-05	5.91166E-06	4.51336E-05	1.79686E-05
	M/LH2O	-0.	2.86266E-03	3.28159E-04	2.50539E-03	9.97444E-04
MG++	MOLES	-0.	3.22042E-03	4.79902E-03	6.72081E-03	2.80560E-01
	MFRAC	-0.	1.97999E-05	5.94911E-05	1.80544E-05	2.33603E-04
	M/LH2O	-0.	1.09910E-03	3.30238E-03	1.00221E-03	1.29674E-02
SO4=	MOLES	-0.	1.46831E-03	3.14022E-04	3.70959E-03	2.15801E-01
	MFRAC	-0.	9.02749E-06	3.89278E-06	9.96523E-06	1.79696E-04
	M/LH2O	-0.	5.01120E-04	2.16090E-04	5.53174E-04	9.97499E-03
HPO4=	MOLES	-0.	3.04181E-03	6.50542E-04	7.68495E-03	1.07900E 00
	MFRAC	-0.	1.87017E-05	8.06446E-06	2.06444E-05	8.98476E-04
	M/LH2O	-0.	1.03814E-03	4.47662E-04	1.14598E-03	4.98748E-02
UREA	MOLES	-0.	1.08012E-02	5.35699E-03	2.47206E-02	7.97510E-02
	MFRAC	-0.	6.64080E-05	6.64080E-05	6.64080E-05	6.64080E-05
	M/LH2O	-0.	3.68634E-03	3.68634E-03	3.68634E-03	3.68634E-03
GLUCOS	MOLES	-0.	1.26018E-02	6.25003E-03	2.88417E-02	9.30460E-02
	MFRAC	-0.	7.74787E-05	7.74787E-05	7.74787E-05	7.74787E-05
	M/LH2O	-0.	4.30088E-03	4.30088E-03	4.30088E-03	4.30088E-03
LACTIC	MOLES	-0.	2.13846E-02	6.36458E-03	5.14218E-02	5.92364E-03
	MFRAC	-0.	1.31476E-04	8.63365E-05	1.38136E-04	4.93257E-06
	M/LH2O	-0.	7.29832E-03	4.79258E-03	7.66802E-03	2.73809E-04
HCO3-	MOLES	-0.	8.75668E-02	3.28048E-02	2.10566E-01	2.06168E-01
	MFRAC	-0.	5.38381E-04	4.36666E-04	5.65652E-04	1.71674E-04
	M/LH2O	-0.	2.98858E-02	2.25742E-02	3.13996E-02	9.52971E-03
H2CO3	MOLES	-0.	6.44549E-06	3.19673E-06	1.47518E-05	4.75907E-05
	MFRAC	-0.	3.96284E-08	3.96284E-08	3.96284E-08	3.96284E-08
	M/LH2O	-0.	2.19979E-06	2.19979E-06	2.19979E-06	2.19979E-06
CO3=	MOLES	-0.	1.18740E-04	2.92106E-05	2.99989E-04	7.74980E-05
	MFRAC	-0.	7.30039E-07	3.62110E-07	8.05872E-07	6.45320E-08
	M/LH2O	-0.	4.05248E-05	2.01009E-05	4.47343E-05	3.58220E-06
PROTN	MOLES	-0.	9.96000E-03	5.31130E-02	2.68830E-02	1.14374E 00
	MFRAC	-0.	6.12364E-05	6.58379E-04	7.22089E-05	9.52304E-04
	M/LH2O	-0.	3.39926E-03	3.65469E-02	4.00835E-03	5.28673E-02
HB4	MOLES	-0.	-0.	9.15510E-04	-0.	-0.
	MFRAC	-0.	-0.	1.13491E-05	-0.	-0.
	M/LH2O	-0.	-0.	6.29996E-04	-0.	-0.
HB4O2	MOLES	-0.	-0.	1.55182E-03	-0.	-0.
	MFRAC	-0.	-0.	1.92372E-05	-0.	-0.
	M/LH2O	-0.	-0.	1.06786E-03	-0.	-0.
HB4O4	MOLES	-0.	-0.	1.05173E-03	-0.	-0.
	MFRAC	-0.	-0.	1.30377E-05	-0.	-0.
	M/LH2O	-0.	-0.	7.23730E-04	-0.	-0.
HB4O6	MOLES	-0.	-0.	4.26832E-04	-0.	-0.
	MFRAC	-0.	-0.	5.29123E-06	-0.	-0.
	M/LH2O	-0.	-0.	2.93718E-04	-0.	-0.
HB4O8	MOLES	-0.	-0.	6.66411E-03	-0.	-0.
	MFRAC	-0.	-0.	8.26118E-05	-0.	-0.
	M/LH2O	-0.	-0.	4.58582E-03	-0.	-0.

Generally speaking, however, a loss of extracellular fluid will involve both plasma and interstitial fluid, which are very similar except for their protein content. Therefore, when fluid, say, at some protein concentration midway between plasma and interstitial fluid is infused (or lost), this infusion (or loss) will spread into both compartments. Thus, in Fig. 2D and Table X, we have the case where all components of the interstitial fluid except protein are decreased (-20 per cent). The result is a nonisotonic contraction where the intracellular spaces are not greatly affected but the loss of volume is shared between interstitial and plasma spaces. There is a very small shift of electrolytes extracellularly to make up the new charge balance (since protein was not lost), but very little is required since the protein content of interstitial fluid is relatively very small. In summary, mathematically speaking, and before the kidney or compensatory mechanisms take over, if the fluid lost is identical in every respect to that in the compartment from which it is lost, that compartment alone will be affected.

INFUSIONS OF ISOTONIC AND HYPERTONIC NaCl SOLUTIONS

In conjunction with Drs. J. V. Maloney, Jr., and G. B. Bradham at the University of California at Los Angeles,

Table X

NONISOTONIC CONTRACTION

TABLE X LOSS OF INTERSTITIAL FLUID BUT NOT PROTEIN (FIG. 20)

		AIR	PLASMA	RED CELLS	INTERSTITIAL	INTRACELL
X-BAR		1.00062E 03	1.40203E 02	8.05283E 01	3.95889E 02	1.19988E 03
PH		-0.	7.37436E 00	7.19613E 00	7.39931E 00	6.82191E 00
O2	MOLES	5.27412E 01	1.31056E-04	7.90540E-05	3.70060E-04	1.83080E-03
	MFRAC	5.27086E-02	9.34758E-07	9.81702E-07	9.34758E-07	1.52582E-06
	M/LH2O	0.	5.18891E-05	5.44949E-05	5.18891E-05	8.46994E-05
CO2	MOLES	6.09738E 01	3.90758E-03	2.24439E-03	1.10337E-02	3.34416E-02
	MFRAC	6.09361E-02	2.78708E-05	2.78708E-05	2.78708E-05	2.78708E-05
	M/LH2O	0.	1.54713E-03	1.54713E-03	1.54713E-03	1.54713E-03
N2	MOLES	8.25800E 02	1.14893E-03	1.08800E-03	3.24419E-03	1.62113E-02
	MFRAC	8.25289E-01	8.19471E-06	1.35108E-05	8.19471E-06	1.35108E-05
	M/LH2O	0.	4.54896E-04	7.49993E-04	4.54894E-04	7.49993E-04
H2O	MOLES	6.11043E 01	1.39393E 02	8.00631E 01	3.93602E 02	1.19295E 03
	MFRAC	6.10664E-02	9.94223E-01	9.94223E-01	9.94223E-01	9.94223E-01
	M/LH2O	0.	5.51900E 01	5.51900E 01	5.51900E 01	5.51900E 01
H+	MOLES	-0.	1.06663E-07	9.23495E-08	2.84365E-07	3.25717E-06
	MFRAC	-0.	7.60776E-10	1.14680E-09	7.18295E-10	2.71458E-09
	M/LH2O	-0.	4.22312E-08	6.36594E-08	3.98731E-08	1.50688E-07
OH-	MOLES	-0.	1.43260E-06	5.45866E-07	4.28464E-06	3.43604E-06
	MFRAC	-0.	1.02180E-08	6.77857E-09	1.08223E-08	2.86366E-09
	M/LH2O	-0.	5.67210E-07	3.76283E-07	6.00755E-07	1.58963E-07
CL-	MOLES	-0.	2.68365E-01	1.02255E-01	8.02590E-01	8.71102E-02
	MFRAC	-0.	1.91411E-03	1.26981E-03	2.02731E-03	7.25991E-05
	M/LH2O	-0.	1.06256E-01	7.04878E-02	1.12537E-01	4.03003E-03
NA+	MOLES	-0.	3.88152E-01	3.88422E-02	1.03489E 00	2.14692E-01
	MFRAC	-0.	2.76849E-03	4.82342E-04	2.61409E-03	1.78928E-04
	M/LH2O	-0.	1.53681E-01	2.67751E-02	1.45110E-01	9.93242E-03
K+	MOLES	-0.	1.09892E-02	1.99402E-01	2.86951E-02	3.45269E 00
	MFRAC	-0.	7.83806E-05	2.47618E-03	7.24828E-05	2.87753E-03
	M/LH2O	-0.	4.35096E-03	1.37454E-01	4.02357E-03	1.59734E-01
CA++	MOLES	-0.	7.36598E-03	4.75212E-04	1.79128E-02	2.14907E-02
	MFRAC	-0.	5.25378E-05	5.90118E-06	4.52471E-05	1.79107E-05
	M/LH2O	-0.	2.91641E-03	3.27579E-04	2.51169E-03	9.94234E-04
MG++	MOLES	-0.	2.83881E-03	4.80029E-03	7.19257E-03	2.80448E-01
	MFRAC	-0.	2.02478E-05	5.96101E-05	1.81682E-05	2.33730E-04
	M/LH2O	-0.	1.12397E-03	3.30899E-03	1.00853E-03	1.29745E-02
SO4=	MOLES	-0.	1.23951E-03	3.13315E-04	3.92620E-03	2.15814E-01
	MFRAC	-0.	8.84080E-06	3.89074E-06	9.91742E-06	1.79863E-04
	M/LH2O	-0.	4.90759E-04	2.15978E-04	5.50523E-04	9.98430E-03
HPO4=	MOLES	-0.	2.56774E-03	6.49054E-04	8.13341E-03	1.07903E 00
	MFRAC	-0.	1.83144E-05	8.35996E-06	2.05447E-05	8.99281E-04
	M/LH2O	-0.	1.01664E-03	4.47414E-04	1.14045E-03	4.99197E-02
UREA	MOLES	-0.	9.31060E-03	5.34770E-03	2.62901E-02	7.96814E-02
	MFRAC	-0.	6.64078E-05	6.64078E-05	6.64078E-05	6.64078E-05
	M/LH2O	-0.	3.68634E-03	3.68634E-03	3.68634E-03	3.68634E-03
GLUCOS	MOLES	-0.	1.08627E-02	6.23920E-03	3.06728E-02	9.29647E-02
	MFRAC	-0.	7.74784E-05	7.74784E-05	7.74784E-05	7.74784E-05
	M/LH2O	-0.	4.30088E-03	4.30088E-03	4.30088E-03	4.30088E-03
LACTIC	MOLES	-0.	1.82472E-02	6.95276E-03	5.45714E-02	5.92298E-03
	MFRAC	-0.	1.30148E-04	8.63396E-05	1.37845E-04	4.93632E-06
	M/LH2O	-0.	7.22462E-03	4.79276E-03	7.65189E-03	2.74018E-04
HCO3-	MOLES	-0.	7.47245E-02	3.27510E-02	2.23476E-01	2.06156E-01
	MFRAC	-0.	5.32972E-04	4.06702E-04	5.64492E-04	1.71814E-04
	M/LH2O	-0.	2.95856E-02	2.25763E-02	3.13354E-02	9.53752E-03
H2CO3	MOLES	-0.	5.55601E-06	3.19119E-06	1.56884E-05	4.75491E-05
	MFRAC	-0.	3.96283E-08	3.96283E-08	3.96283E-08	3.96283E-08
	M/LH2O	-0.	2.19979E-06	2.19979E-06	2.19979E-06	2.19979E-06
CO3=	MOLES	-0.	1.00308E-04	2.91654E-05	3.17730E-04	7.75573E-05
	MFRAC	-0.	7.15446E-07	3.62176E-07	8.02573E-07	6.46376E-08
	M/LH2O	-0.	3.97149E-05	2.01046E-05	4.45514E-05	3.58808E-06
PROTN	MOLES	-0.	9.96000E-03	5.31130E-02	3.36030E-02	1.14374E 00
	MFRAC	-0.	7.10397E-05	6.59520E-04	8.48723E-05	9.53212E-04
	M/LH2O	-0.	3.94346E-03	3.66104E-02	4.71132E-03	5.29134E-02
HB4	MOLES	-0.	-0.	9.15375E-04	-0.	-0.
	MFRAC	-0.	-0.	1.13671E-05	-0.	-0.
	M/LH2O	-0.	-0.	6.30997E-04	-0.	-0.
HB4O2	MOLES	-0.	-0.	1.55167E-03	-0.	-0.
	MFRAC	-0.	-0.	1.92686E-05	-0.	-0.
	M/LH2O	-0.	-0.	1.06961E-03	-0.	-0.
HB4O4	MOLES	-0.	-0.	1.05167E-03	-0.	-0.
	MFRAC	-0.	-0.	1.30597E-05	-0.	-0.
	M/LH2O	-0.	-0.	7.24952E-04	-0.	-0.
HB4O6	MOLES	-0.	-0.	4.26832E-04	-0.	-0.
	MFRAC	-0.	-0.	5.30040E-06	-0.	-0.
	M/LH2O	-0.	-0.	2.94229E-04	-0.	-0.
HB4O8	MOLES	-0.	-0.	6.66645E-03	-0.	-0.
	MFRAC	-0.	-0.	8.27592E-05	-0.	-0.
	M/LH2O	-0.	-0.	4.59402E-03	-0.	-0.

radioisotopic experiments, measuring the total body response to various infusions, were undertaken with nephrectomized dogs. Twenty-two dogs were used, seven for control and five each for infusion with isotonic NaCl, hypertonic NaCl, and hypertonic $NaHCO_3$. The experimental method and results have been reported in a paper by Bradham, et al. [1], where emphasis is placed on the clinical procedure and the results are presented from the point of view of the clinician.

Figure 3 and Tables XI-XIV present the results of the 22 experiments for comparision between the computer and the laboratory.

Figure 3B and Table XII are the computed results of infusion of 20 ml/kg of 0.9 per cent NaCl (isotonic). Figure 3F gives the average of the response of five animals with bilateral nephrectomy and splenectomy to the same infusion. Measurements were made at 30-min intervals, equilibration of the isotopes required 2-3 hr.

Isotonic saline in both the dog and the computed human results causes a general dehydration of the intracellular spaces. Extracellular water increases by more than the total injection--4 per cent more in the model, evidently due to the active sodium pump which concentrates the Na^+ in extracellular spaces and shifts water as well in order to maintain

equal osmolarity. Also, the effect is to dehydrate muscle tissue in preference to red cells--in fact, for isotonic saline the red cells increase slightly in volume (1 per cent).

The computed pH of the entire system drops slightly but uniformly throughout; the Gibbs-Donnan gradient as measured by Cl^- concentration remains approximately the same.

In contrast, the hypertonic NaCl solution moves a great deal more water into the extracellular spaces (Fig. 3C and Table XIII). The infusion was 10 ml/kg of 0.892 M NaCl, approximately 5.8 times the isotonic concentration. With this infusion (700 ml total) the extracellular spaces increased approximately 2800 ml, four times the infusion. Intracellular spaces decreased in volume; muscle tissue more, relative to the red cells. The computed pH of all compartments dropped approximately 0.02. Figure 3G shows a very similar response in the average of five animals.

Hypotonic NaCl solutions could be expected to affect the system in an opposite manner than the hypertonic, but in the model such is not entirely the case. Intracellular spaces increase in volume (Fig. 3A, and Table XI), but so do the extracellular, more in the nature of overhydration. Na^+ concentration decreases in all compartments, but like the hypertonic case, the pH also decreases throughout. This

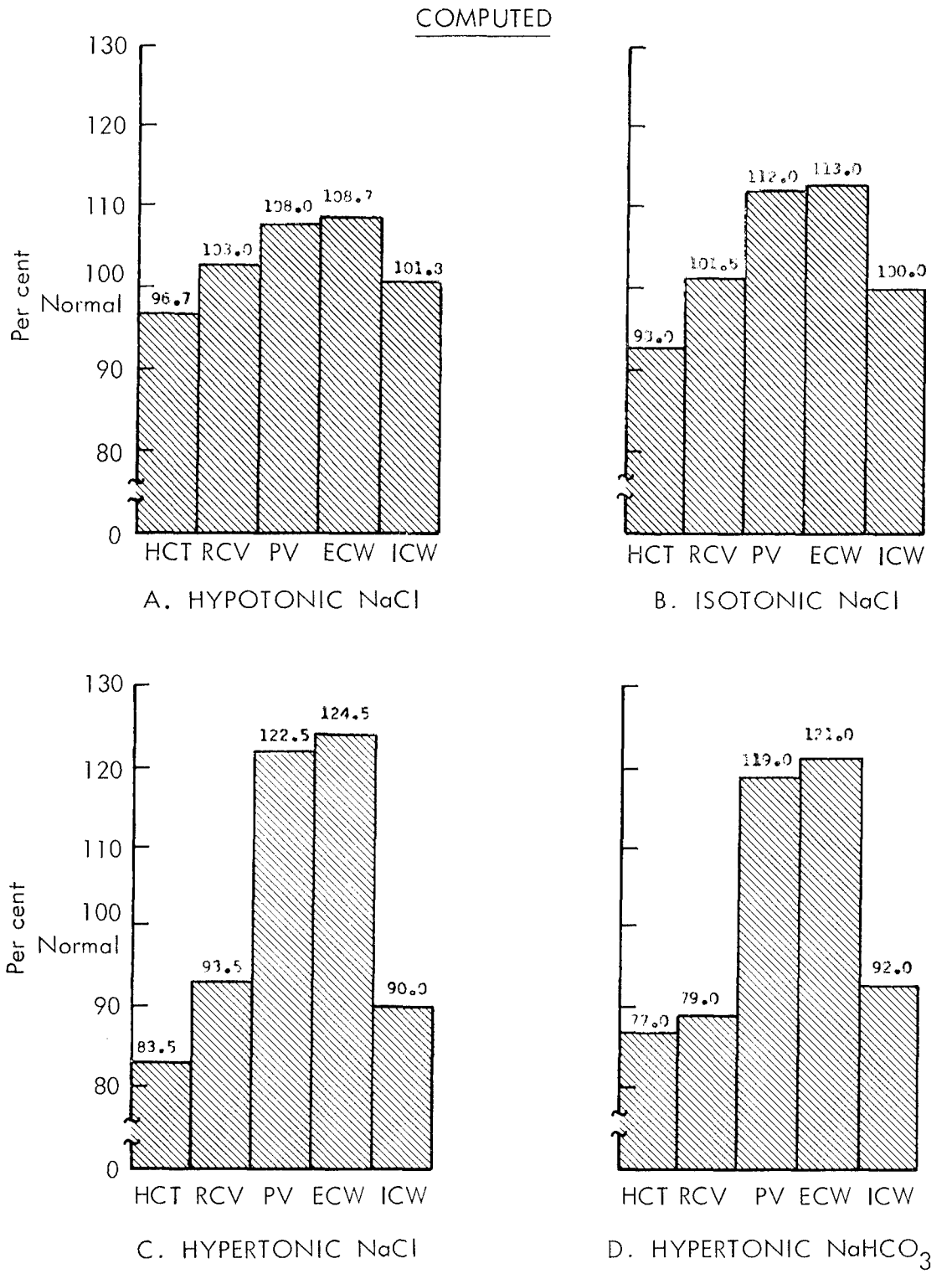
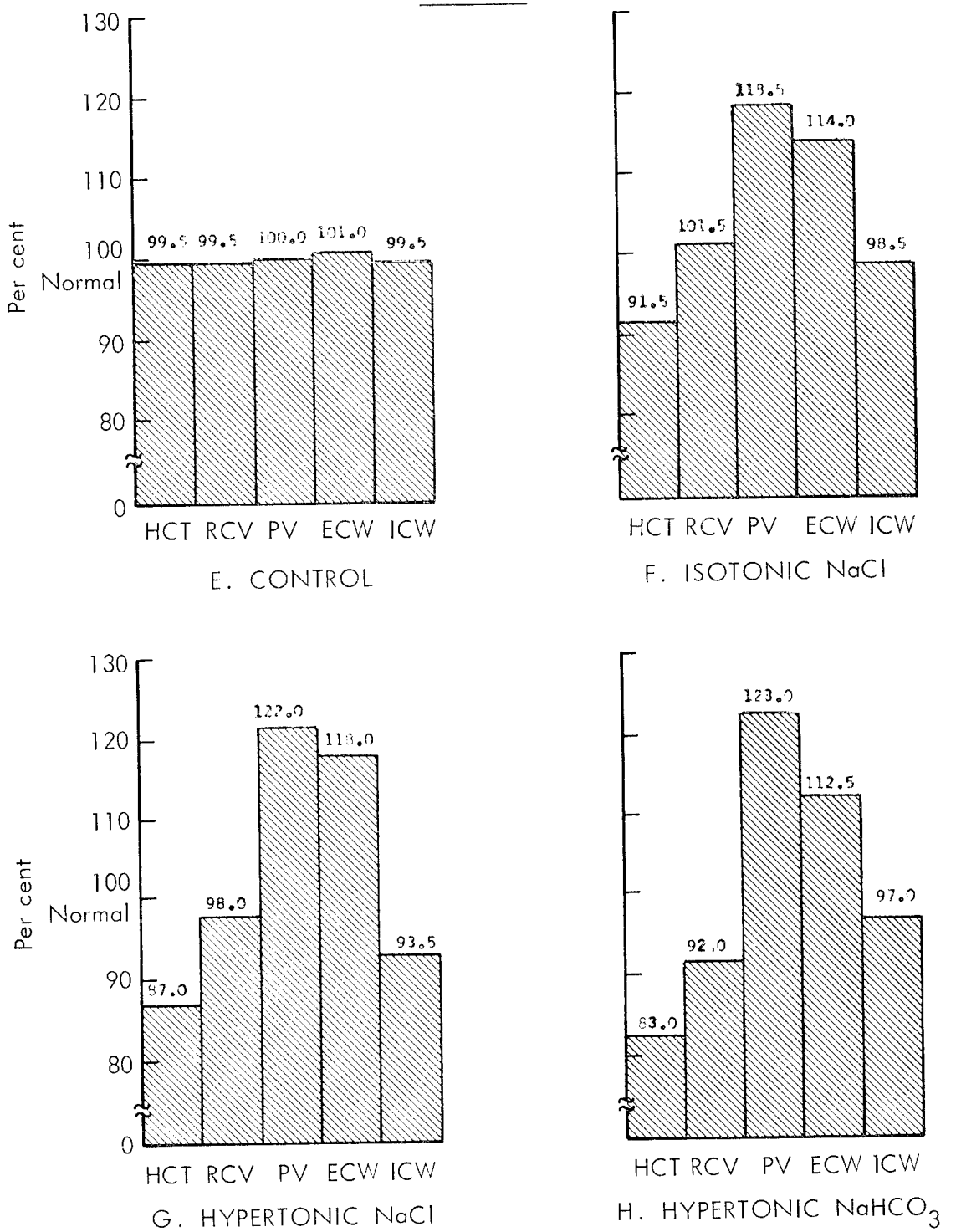


Fig. 3—Nephrectomized dog experiments (computed)

IN VIVO



HCT = Hematocrit
RCV = Red cell volume
PV = Plasma
ECW = Extracellular water
ICW = Intracellular water

Fig. 3—Nephrectomized dog experiments (in vivo)

Table XI

HYPOTONIC NaCl

TABLE XI 20ML/KG OF 0.077 M NACL (FIG. 3A)

		AIR	PLASMA	RED CELLS	INTERSTITIAL	INTRACELL
X-BAR		1.00062E 03	1.76029E 02	8.26608E 01	5.06040E 02	1.22230E 03
PH		-0.	7.35919E 00	7.17444E 00	7.37541E 00	6.79858E 00
O2	MOLES	5.27417E 01	1.64545E-04	8.11488E-05	4.73028E-04	1.86502E-03
	MFRAC	5.27088E-02	9.34764E-07	9.81708E-07	9.34764E-07	1.52583E-06
	M/LH2O	0.	5.18832E-05	5.44888E-05	5.18832E-05	8.46898E-05
CO2	MOLES	6.09709E 01	4.90581E-03	2.30370E-03	1.41030E-02	3.40647E-02
	MFRAC	6.09328E-02	2.78693E-05	2.78693E-05	2.78693E-05	2.78693E-05
	M/LH2O	0.	1.54686E-03	1.54686E-03	1.54686E-03	1.54686E-03
N2	MOLES	8.25800E 02	1.44250E-03	1.11681E-03	4.14683E-03	1.65141E-02
	MFRAC	8.25285E-01	8.19667E-06	1.35107E-05	8.19667E-06	1.35107E-05
	M/LH2O	0.	4.54837E-04	7.49900E-04	4.54837E-04	7.49900E-04
H2O	MOLES	6.11118E 01	1.75033E 02	8.21931E 01	5.03177E 02	1.21538E 03
	MFRAC	6.10737E-02	9.94341E-01	9.94341E-01	9.94341E-01	9.94341E-01
	M/LH2O	0.	5.51900E 01	5.51900E 01	5.51900E 01	5.51900E 01
H+	MOLES	-0.	1.39978E-07	9.96619E-08	3.84095E-07	3.50162E-06
	MFRAC	-0.	7.95197E-10	1.20567E-09	7.59021E-10	2.86478E-09
	M/LH2O	-0.	4.41367E-08	6.69197E-08	4.21288E-08	1.59007E-07
OH-	MOLES	-0.	1.72102E-06	5.33023E-07	5.18331E-06	3.31712E-06
	MFRAC	-0.	9.77690E-09	6.44832E-09	1.02429E-08	2.71384E-09
	M/LH2O	-0.	5.42658E-07	3.57938E-07	5.68521E-07	1.50629E-07
CL-	MOLES	-0.	3.39822E-01	1.05248E-01	1.02347E 00	8.86419E-02
	MFRAC	-0.	1.93049E-03	1.27325E-03	2.02250E-03	7.25207E-05
	M/LH2O	-0.	1.07150E-01	7.06704E-02	1.12257E-01	4.02519E-03
NA+	MOLES	-0.	4.73873E-01	3.89955E-02	1.30039E 00	2.14714E-01
	MFRAC	-0.	2.69202E-03	4.71753E-04	2.56974E-03	1.75664E-04
	M/LH2O	-0.	1.49418E-01	2.61842E-02	1.42631E-01	9.75007E-03
K+	MOLES	-0.	1.34009E-02	1.99962E-01	3.60159E-02	3.44912E 00
	MFRAC	-0.	7.61289E-05	2.41937E-03	7.11719E-05	2.82183E-03
	M/LH2O	-0.	4.22546E-03	1.34268E-01	3.95033E-03	1.56623E-01
CA++	MOLES	-0.	8.57866E-03	4.57775E-04	2.17072E-02	2.07010E-02
	MFRAC	-0.	4.87344E-05	5.53799E-06	4.28962E-05	1.69362E-05
	M/LH2O	-0.	2.70496E-03	3.07381E-04	2.38091E-03	9.40026E-04
MG++	MOLES	-0.	3.42341E-03	4.78813E-03	9.02522E-03	2.79723E-01
	MFRAC	-0.	1.94480E-05	5.79250E-05	1.78350E-05	2.28850E-04
	M/LH2O	-0.	1.07944E-03	3.21537E-03	9.89915E-04	1.27021E-02
SO4=	MOLES	-0.	1.55663E-03	3.17567E-04	4.90537E-03	2.15442E-01
	MFRAC	-0.	8.83170E-06	3.84180E-06	9.69363E-06	1.76260E-04
	M/LH2O	-0.	4.90195E-04	2.13236E-04	5.38036E-04	9.78315E-03
HPO4=	MOLES	-0.	3.22375E-03	6.58518E-04	1.01719E-02	1.07825E 00
	MFRAC	-0.	1.83137E-05	7.96651E-06	2.01011E-05	8.82146E-04
	M/LH2O	-0.	1.01649E-03	4.42174E-04	1.11569E-03	4.89627E-02
UREA	MOLES	-0.	1.12339E-02	5.27531E-03	3.22948E-02	7.80055E-02
	MFRAC	-0.	6.38187E-05	6.38187E-05	6.38187E-05	6.38187E-05
	M/LH2O	-0.	3.54220E-03	3.54220E-03	3.54220E-03	3.54220E-03
GLUCOS	MOLES	-0.	1.31067E-02	6.15473E-03	3.76786E-02	9.10095E-02
	MFRAC	-0.	7.44577E-05	7.44577E-05	7.44577E-05	7.44577E-05
	M/LH2O	-0.	4.13270E-03	4.13270E-03	4.13270E-03	4.13270E-03
LACTIC	MOLES	-0.	2.15063E-02	6.66081E-03	6.47721E-02	5.60988E-03
	MFRAC	-0.	1.22175E-04	8.05800E-05	1.27998E-04	4.58962E-06
	M/LH2O	-0.	6.78120E-03	4.47252E-03	7.10441E-03	2.54742E-04
HCO3-	MOLES	-0.	8.97634E-02	3.19788E-02	2.70347E-01	1.99011E-01
	MFRAC	-0.	5.09935E-04	3.86867E-04	5.34260E-04	1.62817E-04
	M/LH2O	-0.	2.83035E-02	2.14727E-02	2.96525E-02	9.03701E-03
H2CO3	MOLES	-0.	6.97618E-06	3.27592E-06	2.00548E-05	4.84407E-05
	MFRAC	-0.	3.96309E-08	3.96309E-08	3.96309E-08	3.96309E-08
	M/LH2O	-0.	2.19967E-06	2.19967E-06	2.19967E-06	2.19967E-06
CO3=	MOLES	-0.	1.15280E-04	2.70870E-05	3.63745E-04	7.09439E-05
	MFRAC	-0.	6.54892E-07	3.27689E-07	7.18806E-07	5.80414E-08
	M/LH2O	-0.	3.63492E-05	1.81881E-05	3.98966E-05	3.22153E-06
PROTN	MOLES	-0.	9.96000E-03	5.31100E-02	3.36000E-02	1.14374E 00
	MFRAC	-0.	5.65816E-05	6.42505E-04	6.63979E-05	9.35729E-04
	M/LH2O	-0.	3.14051E-03	3.56616E-02	3.68535E-03	5.19368E-02
HB4	MOLES	-0.	-0.	9.91426E-04	-0.	-0.
	MFRAC	-0.	-0.	1.19939E-05	-0.	-0.
	M/LH2O	-0.	-0.	6.65710E-04	-0.	-0.
HB4O2	MOLES	-0.	-0.	1.63571E-03	-0.	-0.
	MFRAC	-0.	-0.	1.97882E-05	-0.	-0.
	M/LH2O	-0.	-0.	1.09833E-03	-0.	-0.
HB4O4	MOLES	-0.	-0.	1.07904E-03	-0.	-0.
	MFRAC	-0.	-0.	1.30538E-05	-0.	-0.
	M/LH2O	-0.	-0.	7.24538E-04	-0.	-0.
HB4O6	MOLES	-0.	-0.	4.26245E-04	-0.	-0.
	MFRAC	-0.	-0.	5.15655E-06	-0.	-0.
	M/LH2O	-0.	-0.	2.86209E-04	-0.	-0.
HB4O8	MOLES	-0.	-0.	6.47758E-03	-0.	-0.
	MFRAC	-0.	-0.	7.83634E-05	-0.	-0.
	M/LH2O	-0.	-0.	4.34949E-03	-0.	-0.

Table XII

ISOTONIC NaCl

TABLE XII: 20ML/KG OF 0.154 M NACL (FIG. 3B)

		AIR	PLASMA	RED CELLS	INTERSTITIAL	INTRACELL
X-BAR		1.00062E 03	1.82574E 02	8.15015E 01	5.26973E 02	1.19620E 03
PH		-0.	7.34869E 00	7.16876E 00	7.36781E 00	6.79233E 00
O2	MOLES	5.27419E 01	1.70666E-04	8.00115E-05	4.92600E-04	1.82522E-03
	MFRAC	5.27096E-02	9.34773E-07	9.81718E-07	9.34773E-07	1.52585E-06
	M/LH2O	0.	5.18894E-05	5.44953E-05	5.18894E-05	8.46999E-05
CO2	MOLES	6.09706E 01	5.08825E-03	2.27140E-03	1.46864E-02	3.33375E-02
	MFRAC	6.09330E-02	2.78694E-05	2.78694E-05	2.78694E-05	2.78694E-05
	M/LH2O	0.	1.54704E-03	1.54704E-03	1.54704E-03	1.54704E-03
N2	MOLES	8.25803E 02	1.49615E-03	1.10115E-03	4.31840E-03	1.61617E-02
	MFRAC	8.25291E-01	8.19473E-06	1.35108E-05	8.19473E-06	1.35108E-05
	M/LH2O	0.	4.54890E-04	7.49987E-04	4.54890E-04	7.49987E-04
H2O	MOLES	6.11047E 01	1.81522E 02	8.10315E 01	5.23934E 02	1.18930E 03
	MFRAC	6.10670E-02	9.94233E-01	9.94233E-01	9.94233E-01	9.94233E-01
	M/LH2O	0.	5.51900E 01	5.51900E 01	5.51900E 01	5.51900E 01
H+	MOLES	-0.	1.47358E-07	9.95455E-08	4.07008E-07	3.47609E-06
	MFRAC	-0.	8.07110E-10	1.22139E-09	7.72351E-10	2.90594E-09
	M/LH2O	-0.	4.48028E-08	6.77997E-08	4.28733E-08	1.61309E-07
OH-	MOLES	-0.	1.75867E-06	5.18727E-07	5.30399E-06	3.19998E-06
	MFRAC	-0.	9.63156E-09	6.36463E-09	1.00650E-08	2.67512E-09
	M/LH2O	-0.	5.34648E-07	3.53301E-07	5.58709E-07	1.48496E-07
CL-	MOLES	-0.	3.65326E-01	1.37766E-01	1.10191E 00	8.99711E-02
	MFRAC	-0.	2.00097E-03	1.32226E-03	2.09102E-03	7.52140E-05
	M/LH2O	-0.	1.11074E-01	7.33990E-02	1.16073E-01	4.17514E-03
NA+	MOLES	-0.	5.00463E-01	3.90753E-02	1.38240E 00	2.13835E-01
	MFRAC	-0.	2.74114E-03	4.79643E-04	2.62328E-03	1.78761E-04
	M/LH2O	-0.	1.52161E-01	2.66139E-02	1.45619E-01	9.92306E-03
K+	MOLES	-0.	1.41939E-02	2.00953E-01	3.83903E-02	3.44496E 00
	MFRAC	-0.	7.77429E-05	2.46563E-03	7.28657E-05	2.87991E-03
	M/LH2O	-0.	4.31552E-03	1.36867E-01	4.04478E-03	1.59864E-01
CA++	MOLES	-0.	8.75180E-03	4.42259E-04	2.23478E-02	1.99028E-02
	MFRAC	-0.	4.79355E-05	5.42639E-06	4.24079E-05	1.66384E-05
	M/LH2O	-0.	2.66090E-03	3.01219E-04	2.35407E-03	9.23597E-04
MG++	MOLES	-0.	3.62194E-03	4.79729E-03	9.63594E-03	2.78905E-01
	MFRAC	-0.	1.98382E-05	5.88613E-05	1.82854E-05	2.33159E-04
	M/LH2O	-0.	1.10122E-03	3.26740E-03	1.01503E-03	1.29427E-02
SO4=	MOLES	-0.	1.64285E-03	3.20241E-04	5.17823E-03	2.15079E-01
	MFRAC	-0.	8.99822E-06	3.92926E-06	9.82636E-06	1.79801E-04
	M/LH2O	-0.	4.99492E-04	2.18114E-04	5.45462E-04	9.98079E-03
HPO4=	MOLES	-0.	3.40999E-03	6.64712E-04	1.07483E-02	1.07748E 00
	MFRAC	-0.	1.86773E-05	8.15582E-06	2.03962E-05	9.00749E-04
	M/LH2O	-0.	1.03678E-03	4.52730E-04	1.13220E-03	5.00007E-02
UREA	MOLES	-0.	1.16504E-02	5.20074E-03	3.36270E-02	7.63315E-02
	MFRAC	-0.	6.38116E-05	6.38116E-05	6.38116E-05	6.38116E-05
	M/LH2O	-0.	3.54219E-03	3.54219E-03	3.54219E-03	3.54219E-03
GLUCOS	MOLES	-0.	1.35926E-02	6.06773E-03	3.92328E-02	8.90564E-02
	MFRAC	-0.	7.44493E-05	7.44493E-05	7.44493E-05	7.44493E-05
	M/LH2O	-0.	4.13269E-03	4.13269E-03	4.13269E-03	4.13269E-03
LACTIC	MOLES	-0.	2.16235E-02	6.37864E-03	6.52217E-02	5.32534E-03
	MFRAC	-0.	1.18436E-04	7.82641E-05	1.23767E-04	4.45188E-06
	M/LH2O	-0.	6.57442E-03	4.34445E-03	6.87030E-03	2.47124E-04
HCO3-	MOLES	-0.	9.17173E-02	3.11211E-02	2.76642E-01	1.91984E-01
	MFRAC	-0.	5.02356E-04	3.81847E-04	5.24944E-04	1.60494E-04
	M/LH2O	-0.	2.78858E-02	2.11964E-02	2.91408E-02	8.90905E-03
H2CO3	MOLES	-0.	7.23482E-06	3.22964E-06	2.08822E-05	4.74015E-05
	MFRAC	-0.	3.96267E-08	3.96267E-08	3.96267E-08	3.96267E-08
	M/LH2O	-0.	2.19968E-06	2.19968E-06	2.19968E-06	2.19968E-06
CO3=	MOLES	-0.	1.16051E-04	2.60213E-05	3.65791E-04	6.74694E-03
	MFRAC	-0.	6.35635E-07	3.19274E-07	6.94135E-07	5.64031E-06
	M/LH2O	-0.	3.52842E-05	1.77229E-05	3.85315E-05	3.13094E-04
PROTN	MOLES	-0.	9.96000E-03	5.31100E-02	3.36000E-02	1.14376E 00
	MFRAC	-0.	5.45531E-05	6.51644E-04	6.37604E-05	9.56163E-04
	M/LH2O	-0.	3.02825E-03	3.61728E-02	3.53934E-03	5.30756E-02
HB4	MOLES	-0.	-0.	1.01218E-03	-0.	-0.
	MFRAC	-0.	-0.	1.24192E-05	-0.	-0.
	M/LH2O	-0.	-0.	6.89392E-04	-0.	-0.
HB4O2	MOLES	-0.	-0.	1.65812E-03	-0.	-0.
	MFRAC	-0.	-0.	2.03447E-05	-0.	-0.
	M/LH2O	-0.	-0.	1.12934E-03	-0.	-0.
HB4O4	MOLES	-0.	-0.	1.08606E-03	-0.	-0.
	MFRAC	-0.	-0.	1.33257E-05	-0.	-0.
	M/LH2O	-0.	-0.	7.39710E-04	-0.	-0.
HB4O6	MOLES	-0.	-0.	4.25979E-04	-0.	-0.
	MFRAC	-0.	-0.	5.22664E-06	-0.	-0.
	M/LH2O	-0.	-0.	2.90131E-04	-0.	-0.
HB4O8	MOLES	-0.	-0.	6.42765E-03	-0.	-0.
	MFRAC	-0.	-0.	7.88654E-05	-0.	-0.
	M/LH2O	-0.	-0.	4.37702E-03	-0.	-0.

Table XIII

HYPERTONIC NaCl

TABLE XIII 10ML/KG OF 0.892 M NACL (FIG. 3C)

		AIR	PLASMA	RED CELLS	INTERSTITIAL	INTRACELL
X-BAR		1.00058E 03	2.01260E 02	7.55971E 01	5.87379E 02	1.08523E 03
PH		-0.	7.33543E 00	7.15735E 00	7.35128E 00	6.77941E 00
O2	MOLES	5.27423E 01	1.88140E-04	7.42181E-05	5.49088E-04	1.65596E-03
	MFRAC	5.27115E-02	9.34811E-07	9.81758E-07	9.34811E-07	1.52591E-06
	M/LH2O	0.	5.19192E-05	5.45266E-05	5.19192E-05	8.47685E-05
CO2	MOLES	6.09713E 01	5.60924E-03	2.10634E-03	1.63706E-02	3.02461E-02
	MFRAC	6.09357E-02	2.78707E-05	2.78707E-05	2.78706E-05	2.78707E-05
	M/LH2O	0.	1.54793E-03	1.54793E-03	1.54793E-03	1.54793E-03
N2	MOLES	8.25801E 02	1.64932E-03	1.02141E-03	4.81357E-03	1.46629E-02
	MFRAC	8.25318E-01	8.19500E-06	1.35113E-05	8.19500E-06	1.35113E-05
	M/LH2O	0.	4.55148E-04	7.50412E-04	4.55148E-04	7.50412E-04
H2O	MOLES	6.10701E 01	1.99993E 02	7.51211E 01	5.83680E 02	1.07840E 03
	MFRAC	6.10345E-02	9.93703E-01	9.93703E-01	9.93703E-01	9.93703E-01
	M/LH2O	0.	5.51900E 01	5.51900E 01	5.51900E 01	5.51900E 01
H+	MOLES	-0.	1.67384E-07	9.47433E-08	4.71010E-07	3.24716E-06
	MFRAC	-0.	8.31679E-10	1.25327E-09	8.01885E-10	2.99213E-09
	M/LH2O	-0.	4.61912E-08	6.96060E-08	4.45365E-08	1.66182E-07
OH-	MOLES	-0.	1.88018E-06	4.68661E-07	5.69119E-06	2.81798E-06
	MFRAC	-0.	9.34203E-09	6.19946E-09	9.68913E-09	2.59667E-09
	M/LH2O	-0.	5.18854E-07	3.44316E-07	5.38132E-07	1.44218E-07
CL-	MOLES	-0.	4.62995E-01	1.15408E-01	1.40146E 00	9.39136E-02
	MFRAC	-0.	2.30048E-03	1.52662E-03	2.38596E-03	8.65376E-05
	M/LH2O	-0.	1.27768E-01	8.47882E-02	1.32515E-01	4.80628E-03
NA+	MOLES	-0.	6.01416E-01	3.93453E-02	1.69248E 00	2.11327E-01
	MFRAC	-0.	2.98826E-03	5.20461E-04	2.88142E-03	1.94730E-04
	M/LH2O	-0.	1.65967E-01	2.89063E-02	1.60033E-01	1.08152E-02
K+	MOLES	-0.	1.71850E-02	2.03859E-01	4.73639E-02	3.43009E 00
	MFRAC	-0.	8.53872E-05	2.59665E-03	8.06361E-05	3.16070E-03
	M/LH2O	-0.	4.74238E-03	1.49771E-01	4.47851E-03	1.75544E-01
CA++	MOLES	-0.	9.29921E-03	3.92082E-04	2.43751E-02	1.73784E-02
	MFRAC	-0.	4.62050E-05	5.18647E-06	4.14980E-05	1.60135E-05
	M/LH2O	-0.	2.56421E-03	2.88055E-04	2.30479E-03	8.89385E-04
MG++	MOLES	-0.	4.35968E-03	4.81793E-03	1.19061E-02	2.75876E-01
	MFRAC	-0.	2.16619E-05	6.37317E-05	2.02699E-05	2.54209E-04
	M/LH2O	-0.	1.20310E-03	3.53964E-03	1.12578E-03	1.41187E-02
SO4=	MOLES	-0.	1.98033E-03	3.27574E-04	6.21706E-03	2.13695E-01
	MFRAC	-0.	9.83965E-06	4.33316E-06	1.05844E-05	1.96912E-04
	M/LH2O	-0.	5.46492E-04	2.40662E-04	5.87855E-04	1.09364E-02
HPO4=	MOLES	-0.	4.12583E-03	6.82470E-04	1.29527E-02	1.07454E 00
	MFRAC	-0.	2.05000E-05	9.32772E-06	2.20516E-05	9.90147E-04
	M/LH2O	-0.	1.13856E-03	5.01397E-04	1.22474E-03	5.49925E-02
UREA	MOLES	-0.	1.30916E-02	4.91747E-03	3.82080E-02	7.05925E-02
	MFRAC	-0.	6.50483E-05	6.50483E-05	6.50483E-05	6.50483E-05
	M/LH2O	-0.	3.61277E-03	3.61277E-03	3.61277E-03	3.61277E-03
GLUCOS	MOLES	-0.	1.52741E-02	5.73724E-03	4.45775E-02	8.23607E-02
	MFRAC	-0.	7.58922E-05	7.58922E-05	7.58922E-05	7.58922E-05
	M/LH2O	-0.	4.21504E-03	4.21504E-03	4.21504E-03	4.21504E-03
LACTIC	MOLES	-0.	2.20022E-02	5.48438E-03	6.65996E-02	4.46291E-03
	MFRAC	-0.	1.09323E-04	7.25475E-05	1.13384E-04	4.11240E-06
	M/LH2O	-0.	6.07175E-03	4.02927E-03	6.29734E-03	2.28402E-04
HCO3-	MOLES	-0.	9.80693E-02	2.81187E-02	2.96850E-01	1.69073E-01
	MFRAC	-0.	4.87277E-04	3.71954E-04	5.05381E-04	1.55794E-04
	M/LH2O	-0.	2.70432E-02	2.06582E-02	2.80687E-02	8.65278E-03
H2CO3	MOLES	-0.	7.97136E-06	2.99420E-06	2.32665E-05	4.29831E-05
	MFRAC	-0.	3.96073E-08	3.96073E-08	3.96073E-08	3.96073E-08
	M/LH2O	-0.	2.19978E-06	2.19978E-06	2.19978E-06	2.19978E-06
CO3=	MOLES	-0.	1.20422E-04	2.29129E-05	3.78055E-04	5.77062E-03
	MFRAC	-0.	5.98342E-07	3.03093E-07	6.43630E-07	5.31741E-06
	M/LH2O	-0.	3.32318E-05	1.68337E-05	3.57470E-05	2.95328E-04
PROTN	MOLES	-0.	9.96000E-03	5.31100E-02	3.36000E-02	1.14374E 00
	MFRAC	-0.	4.94883E-05	7.02540E-04	5.72033E-05	1.05391E-03
	M/LH2O	-0.	2.74856E-03	3.90189E-02	3.17706E-03	5.85340E-02
HB4	MOLES	-0.	-0.	1.05476E-03	-0.	-0.
	MFRAC	-0.	-0.	1.39524E-05	-0.	-0.
	M/LH2O	-0.	-0.	7.74915E-04	-0.	-0.
HB4O2	MOLES	-0.	-0.	1.70340E-03	-0.	-0.
	MFRAC	-0.	-0.	2.25327E-05	-0.	-0.
	M/LH2O	-0.	-0.	1.25146E-03	-0.	-0.
HB4O4	MOLES	-0.	-0.	1.09992E-03	-0.	-0.
	MFRAC	-0.	-0.	1.45498E-05	-0.	-0.
	M/LH2O	-0.	-0.	8.08092E-04	-0.	-0.
HB4O6	MOLES	-0.	-0.	4.25305E-04	-0.	-0.
	MFRAC	-0.	-0.	5.62594E-06	-0.	-0.
	M/LH2O	-0.	-0.	3.12463E-04	-0.	-0.
HB4O8	MOLES	-0.	-0.	6.32660E-01	-0.	-0.
	MFRAC	-0.	-0.	8.36884E-05	-0.	-0.
	M/LH2O	-0.	-0.	4.64803E-03	-0.	-0.

decrease in pH is apparently a function of the water added, as discussed in overhydration above, and is not a function of the NaCl. Corresponding dog experiments were not tried.

$NaHCO_3$ STRESS

Hypertonic infusions of $NaHCO_3$ (10 ml/kg of 0.892 M $NaHCO_3$) were given to five experimental animals in an effort to distinguish the differences between the stress of NaCl and $NaHCO_3$. The effects are quite different, as can be seen in Figs. 3D and 3H and in Table XIV.

The Na^+ and the total volume, of course, go up. The computed pH increases approximately 0.2, since $NaHCO_3$ is alkaline. Intracellular volume decreases, as with the administration of NaCl, but more proportionately than red cell volume, which is opposite to the NaCl effect. In this case, the red cells lost considerably more water (13 per cent) than for NaCl; the muscle tissue less (3 per cent); hematocrit decreased 25 per cent from the normal. Note that in no case does the computer correctly predict the quantitative ECW change. We discuss this below.

Many similar results can be worked out in detail from the computer experiment. For example, whereas the normal intra-extracellular Gibbs-Donnan gradient was 1:28, it is

Table XIV

HYPERTONIC $NaHCO_3$

TABLE XIV 10ML/KG OF 0.892 M NAHCO3 (FIG. 3D)

		AIR	PLASMA	RED CELLS	INTERSTITIAL	INTRACELL
X-BAR		1.00059E 03	1.94048E 02	6.41230E 01	5.69534E 02	1.12176E 03
PH		-0.	7.67191E 00	7.41125E 00	7.68840E 00	7.04766E 00
O2	MOLES	5.27373E 01	1.81380E-04	6.29469E-05	5.32353E-04	1.71153E-03
	MFRAC	5.27062E-02	9.34717E-07	9.81659E-07	9.34717E-07	1.52575E-06
	M/LH2O	0.	5.19135E-05	5.45206E-05	5.19135E-05	8.47393E-05
CO2	MOLES	6.09803E 01	5.40903E-03	1.78741E-03	1.58756E-02	3.12687E-02
	MFRAC	6.09444E-02	2.78747E-05	2.78747E-05	2.78747E-05	2.78747E-05
	M/LH2O	0.	1.54814E-03	1.54814E-03	1.54814E-03	1.54814E-03
N2	MOLES	8.25801E 02	1.59022E-03	8.66378E-04	4.66731E-03	1.51564E-02
	MFRAC	8.25314E-01	8.19496E-06	1.35112E-05	8.19496E-06	1.35112E-05
	M/LH2O	0.	4.55142E-04	7.50402E-04	4.55142E-04	7.50402E-04
H2O	MOLES	6.10709E 01	1.92828E 02	6.37197E 01	5.65952E 02	1.11471E 03
	MFRAC	6.10350E-02	9.93711E-01	9.93711E-01	9.93711E-01	9.93711E-01
	M/LH2O	0.	5.51900E 01	5.51900E 01	5.51900E 01	5.51900E 01
H+	MOLES	-0.	7.43696E-08	4.47872E-08	2.10139E-07	1.80981E-06
	MFRAC	-0.	3.83253E-10	6.98459E-10	3.68966E-10	1.61336E-09
	M/LH2O	-0.	2.12856E-08	3.87919E-08	2.04921E-08	8.96048E-08
OH-	MOLES	-0.	3.93391E-06	7.13302E-07	1.19932E-05	5.40219E-06
	MFRAC	-0.	2.02729E-08	1.11240E-08	2.10578E-08	4.81581E-09
	M/LH2O	-0.	1.12594E-06	6.17817E-07	1.16954E-06	2.67466E-07
CL-	MOLES	-0.	3.28223E-01	5.95138E-02	1.00064E 00	6.09994E-02
	MFRAC	-0.	1.69145E-03	9.28121E-04	1.75695E-03	5.43782E-05
	M/LH2O	-0.	9.39420E-02	5.15471E-02	9.75795E-02	3.02012E-03
NA+	MOLES	-0.	5.86821E-01	4.08458E-02	1.65824E 00	2.58661E-01
	MFRAC	-0.	3.02410E-03	6.36992E-04	2.91158E-03	2.30585E-04
	M/LH2O	-0.	1.67956E-01	3.53780E-02	1.61707E-01	1.28065E-02
K+	MOLES	-0.	1.38640E-02	1.74981E-01	3.83689E-02	3.47129E 00
	MFRAC	-0.	7.14461E-05	2.72884E-03	6.73689E-05	3.09449E-03
	M/LH2O	-0.	3.96806E-03	1.51558E-01	3.74162E-03	1.71866E-01
CA++	MOLES	-0.	8.00652E-03	4.34376E-04	2.10417E-02	2.19621E-02
	MFRAC	-0.	4.12605E-05	6.77411E-06	3.69455E-05	1.95782E-05
	M/LH2O	-0.	2.29158E-03	3.76229E-04	2.05193E-03	1.08736E-03
MG++	MOLES	-0.	3.02893E-03	4.30712E-03	8.29358E-03	2.81330E-01
	MFRAC	-0.	1.56092E-05	6.71697E-05	1.45621E-05	2.50793E-04
	M/LH2O	-0.	8.66923E-04	3.73055E-03	8.08766E-04	1.39289E-02
SO4=	MOLES	-0.	2.50351E-03	2.49082E-04	7.92788E-03	2.11539E-01
	MFRAC	-0.	1.29015E-05	3.88445E-06	1.39199E-05	1.88578E-04
	M/LH2O	-0.	7.16539E-04	2.15739E-04	7.73134E-04	1.04735E-02
HPO4=	MOLES	-0.	5.24632E-03	5.21973E-04	1.66135E-02	1.06992E 00
	MFRAC	-0.	2.70362E-05	8.14019E-06	2.91704E-05	9.53783E-04
	M/LH2O	-0.	1.50157E-03	4.52100E-04	1.62010E-03	5.29724E-02
UREA	MOLES	-0.	1.26225E-02	4.17139E-03	3.70472E-02	7.29688E-02
	MFRAC	-0.	6.50483E-05	6.50483E-05	6.50483E-05	6.50483E-05
	M/LH2O	-0.	3.61274E-03	3.61274E-03	3.61274E-03	3.61274E-03
GLUCOS	MOLES	-0.	1.47268E-02	4.86644E-03	4.32232E-02	8.51331E-02
	MFRAC	-0.	7.58923E-05	7.58923E-05	7.58923E-05	7.58923E-05
	M/LH2O	-0.	4.21500E-03	4.21500E-03	4.21500E-03	4.21500E-03
LACTIC	MOLES	-0.	2.23173E-02	4.04659E-03	6.80377E-02	4.14760E-03
	MFRAC	-0.	1.15009E-04	6.31068E-05	1.19462E-04	3.69740E-06
	M/LH2O	-0.	6.38750E-03	3.50490E-03	6.63483E-03	2.05351E-04
HCO3-	MOLES	-0.	2.05221E-01	4.28027E-02	6.25648E-01	3.24166E-01
	MFRAC	-0.	1.05758E-03	6.67510E-04	1.09853E-03	2.88980E-04
	M/LH2O	-0.	5.87370E-02	3.70730E-02	6.10114E-02	1.60497E-02
H2CO3	MOLES	-0.	7.68689E-06	2.54012E-06	2.25611E-05	4.44367E-05
	MFRAC	-0.	3.96133E-08	3.96133E-08	3.96133E-08	3.96133E-08
	M/LH2O	-0.	2.20009E-06	2.20009E-06	2.20009E-06	2.20009E-06
CO3=	MOLES	-0.	5.46846E-04	6.25835E-05	1.73170E-03	2.05195E-04
	MFRAC	-0.	2.81809E-06	9.75992E-07	3.04056E-06	1.82922E-07
	M/LH2O	-0.	1.56515E-04	5.42059E-05	1.68870E-04	1.01593E-05
PROTN	MOLES	-0.	9.96000E-03	5.31100E-02	3.36000E-02	1.14374E 00
	MFRAC	-0.	5.13275E-05	8.28253E-04	5.89956E-05	1.01959E-03
	M/LH2O	-0.	2.85069E-03	4.60005E-02	3.27657E-03	5.66274E-02
HB4	MOLES	-0.	-0.	4.73806E-04	-0.	-0.
	MFRAC	-0.	-0.	7.38932E-06	-0.	-0.
	M/LH2O	-0.	-0.	4.10381E-04	-0.	-0.
HB402	MOLES	-0.	-0.	9.88385E-04	-0.	-0.
	MFRAC	-0.	-0.	1.54139E-05	-0.	-0.
	M/LH2O	-0.	-0.	8.56076E-04	-0.	-0.
HB404	MOLES	-0.	-0.	8.24392E-04	-0.	-0.
	MFRAC	-0.	-0.	1.28564E-05	-0.	-0.
	M/LH2O	-0.	-0.	7.14036E-04	-0.	-0.
HB406	MOLES	-0.	-0.	4.11752E-04	-0.	-0.
	MFRAC	-0.	-0.	6.42128E-06	-0.	-0.
	M/LH2O	-0.	-0.	3.56633E-04	-0.	-0.
HB408	MOLES	-0.	-0.	7.91167E-03	-0.	-0.
	MFRAC	-0.	-0.	1.23383E-04	-0.	-0.
	M/LH2O	-0.	-0.	6.85259E-03	-0.	-0.

now 1:32, as measured by the Cl^- ion; the plasma-red cell apparent Na^+ gradient is now 1:12.6, a reduction from 14.6 due, no doubt, to the increased Gibbs-Donnan effect.

The computed saturation of hemoglobin goes up from 74 per cent to 83 per cent because of the shift in pH. Mg^{++} and Ca^{++}, because of the double-ion effect, decrease almost 20 per cent in concentration in the plasma, while K^+ concentration goes down about 10 per cent in response to the increased Donnan gradient. HCO_3^- increases about 65 per cent in the cells, but almost 95 per cent in extracellular fluid due to the change in pH and the Donnan gradient.

The computed isotonic $NaHCO_3$ (Table XV) and hypotonic $NaHCO_3$ (Table XVI) results are different only in degree from hypertonic. This conclusion may be significant inasmuch as hypotonic NaCl gives an opposite result from hypertonic. Of course, the HCO_3^- is strongly buffered and should have less direct effect than Cl^-.

COMPARISON WITH ANIMAL EXPERIMENTS

It is evident that a great deal more detailed information is available from the computer than can be obtained easily from the laboratory. In order to check the computer, it would be very convenient to know, for example, how the

Table XV

ISOTONIC $NaHCO_3$

TABLE XV 20ML/KG OF 0.154 M NAHCO3

		AIR	PLASMA	RED CELLS	INTERSTITIAL	INTRACELL
X-BAR		1.00062E 03	1.79686E 02	7.54611E 01	5.19377E 02	1.21273E 03
PH		-0.	7.49393E 00	7.27955E 00	7.51340E 00	6.90947E 00
O2	MOLES	5.27392E 01	1.67957E-04	7.40776E-05	4.85473E-04	1.85033E-03
	MFRAC	5.27066E-02	9.34723E-07	9.81665E-07	9.34723E-07	1.52576E-06
	M/LH2O	0.	5.18864E-05	5.44921E-05	5.18864E-05	8.46950E-05
CO2	MOLES	6.09747E 01	5.00808E-03	2.10320E-03	1.44757E-02	3.38002E-02
	MFRAC	6.09370E-02	2.78713E-05	2.78713E-05	2.78713E-05	2.78713E-05
	M/LH2O	0.	1.54713E-03	1.54713E-03	1.54713E-03	1.54713E-03
N2	MOLES	8.25800E 02	1.47248E-03	1.31954E-03	4.25614E-03	1.63849E-02
	MFRAC	8.25289E-01	8.19471E-06	1.35108E-05	8.19471E-06	1.35108E-05
	M/LH2O	0.	4.54888E-04	7.49983E-04	4.54888E-04	7.49983E-04
H2O	MOLES	6.11050E 01	1.78651E 02	7.50263E 01	5.16384E 02	1.20574E 03
	MFRAC	6.10673E-02	9.94237E-01	9.94237E-01	9.94237E-01	9.94237E-01
	M/LH2O	0.	5.51900E 01	5.51900E 01	5.51900E 01	5.51900E 01
H+	MOLES	-0.	1.03801E-07	7.14154E-08	2.86880E-07	2.69101E-06
	MFRAC	-0.	5.77680E-10	9.46387E-10	5.52355E-10	2.21897E-09
	M/LH2O	-0.	3.20670E-08	5.25338E-08	3.06612E-08	1.23175E-07
OH-	MOLES	-0.	2.41800E-06	6.19847E-07	7.30962E-06	4.24855E-06
	MFRAC	-0.	1.34568E-08	8.21412E-09	1.40738E-08	3.50331E-09
	M/LH2O	-0.	7.46987E-07	4.55965E-07	7.81236E-07	1.94468E-07
CL-	MOLES	-0.	3.20862E-01	8.22519E-02	9.69965E-01	7.62981E-02
	MFRAC	-0.	1.78568E-03	1.08999E-03	1.86756E-03	6.29145E-05
	M/LH2O	-0.	9.91230E-02	6.05053E-02	1.03668E-01	3.49238E-03
NA+	MOLES	-0.	4.95189E-01	3.93771E-02	1.36868E 00	2.32527E-01
	MFRAC	-0.	2.75586E-03	5.21820E-04	2.63523E-03	1.91739E-04
	M/LH2O	-0.	1.52977E-01	2.89662E-02	1.46282E-01	1.06434E-02
K+	MOLES	-0.	1.29836E-02	1.07210E-01	3.51458E-02	3.46316E 00
	MFRAC	-0.	7.22570E-05	2.48088E-03	6.76692E-05	2.85568E-03
	M/LH2O	-0.	4.01098E-03	1.37713E-01	3.75631E-03	1.58519E-01
CA++	MOLES	-0.	8.19819E-03	4.56770E-04	2.09302E-02	2.18596E-02
	MFRAC	-0.	4.56250E-05	6.05304E-06	4.02986E-05	1.80251E-05
	M/LH2O	-0.	2.53264E-03	3.36004E-04	2.23697E-03	1.00057E-03
MG++	MOLES	-0.	3.11258E-03	4.54542E-03	8.27923E-03	2.81023E-01
	MFRAC	-0.	1.73223E-05	6.02353E-05	1.59407E-05	2.31728E-04
	M/LH2O	-0.	9.61561E-04	3.34366E-03	8.84867E-04	1.28632E-02
SO4=	MOLES	-0.	1.80957E-03	2.83153E-04	5.72113E-03	2.14406E-01
	MFRAC	-0.	1.00707E-05	3.75230E-06	1.10154E-05	1.76797E-04
	M/LH2O	-0.	5.59024E-04	2.08290E-04	6.11462E-04	9.81397E-03
HPO4=	MOLES	-0.	3.76285E-03	5.88794E-04	1.18966E-02	1.07605E 00
	MFRAC	-0.	2.09412E-05	7.80261E-06	2.29056E-05	8.87299E-04
	M/LH2O	-0.	1.16245E-03	4.33122E-04	1.27149E-03	4.92539E-02
UREA	MOLES	-0.	1.14660E-02	4.81529E-03	3.31423E-02	7.73860E-02
	MFRAC	-0.	6.38116E-05	6.38116E-05	6.38116E-05	6.38116E-05
	M/LH2O	-0.	3.54217E-03	3.54217E-03	3.54217E-03	3.54217E-03
GLUCOS	MOLES	-0.	1.33775E-02	5.61803E-03	3.86673E-02	9.02867E-02
	MFRAC	-0.	7.44493E-05	7.44493E-05	7.44493E-05	7.44493E-05
	M/LH2O	-0.	4.13268E-03	4.13268E-03	4.13268E-03	4.13268E-03
LACTIC	MOLES	-0.	2.18167E-02	5.59265E-03	6.59519E-02	5.18782E-03
	MFRAC	-0.	1.21416E-04	7.41129E-05	1.26983E-04	4.27781E-06
	M/LH2O	-0.	6.73978E-03	4.11400E-03	7.04880E-03	2.37461E-04
HCO3-	MOLES	-0.	1.26125E-01	3.71903E-02	3.81275E-01	2.54910E-01
	MFRAC	-0.	7.01918E-04	4.92841E-04	7.34101E-04	2.10196E-04
	M/LH2O	-0.	3.89634E-02	2.73575E-02	4.07499E-02	1.16679E-02
H2CO3	MOLES	-0.	7.12086E-06	2.99048E-06	2.05826E-05	4.80597E-05
	MFRAC	-0.	3.96294E-08	3.96294E-08	3.96294E-08	3.96294E-08
	M/LH2O	-0.	2.19983E-06	2.19983E-06	2.19983E-06	2.19983E-06
CO3=	MOLES	-0.	2.22968E-04	4.01320E-05	7.04936E-04	1.17318E-04
	MFRAC	-0.	1.24088E-06	5.31823E-07	1.35727E-06	9.67388E-08
	M/LH2O	-0.	6.88809E-05	2.95214E-05	7.53421E-05	5.36996E-06
PROTN	MOLES	-0.	9.96000E-03	5.31100E-02	3.36000E-02	1.14374E 00
	MFRAC	-0.	5.54300E-05	7.03806E-04	6.46929E-05	9.43114E-04
	M/LH2O	-0.	3.07691E-03	3.90682E-02	3.59110E-03	5.23522E-02
HB4	MOLES	-0.	-0.	6.82878E-04	-0.	-0.
	MFRAC	-0.	-0.	9.04940E-06	-0.	-0.
	M/LH2O	-0.	-0.	5.02331E-04	-0.	-0.
HB402	MOLES	-0.	-0.	1.27337E-03	-0.	-0.
	MFRAC	-0.	-0.	1.68746E-05	-0.	-0.
	M/LH2O	-0.	-0.	9.36705E-04	-0.	-0.
HB404	MOLES	-0.	-0.	9.49403E-04	-0.	-0.
	MFRAC	-0.	-0.	1.25814E-05	-0.	-0.
	M/LH2O	-0.	-0.	6.98390E-04	-0.	-0.
HB406	MOLES	-0.	-0.	4.23877E-04	-0.	-0.
	MFRAC	-0.	-0.	5.61715E-06	-0.	-0.
	M/LH2O	-0.	-0.	3.11808E-04	-0.	-0.
HB408	MOLES	-0.	-0.	7.28047E-03	-0.	-0.
	MFRAC	-0.	-0.	9.64797E-05	-0.	-0.
	M/LH2O	-0.	-0.	5.35558E-03	-0.	-0.

Table XVI

HYPOTONIC $NaHCO_3$

TABLE XVI 20ML/KG OF 0.077 M NAHCO3

		AIR	PLASMA	RED CELLS	INTERSTITIAL	INTRACELL
X-BAR		1.00062E 03	1.74554E 02	7.92621E 01	5.02038E 02	1.23117E 03
PH		-0.	7.43326E 00	7.23435E 00	7.45368E 00	6.86192E 00
O2	MOLES	5.27401E 01	1.63162E-04	7.78098E-05	4.69272E-04	1.87850E-33
	MFRAC	5.27072E-02	9.34735E-07	9.81677E-07	9.34735E-07	1.52578E-36
	M/LH2O	0.	5.18815E-05	5.46870E-05	5.18815E-05	8.46870E-05
CO2	MOLES	6.09731E 01	4.86689E-03	2.20906E-03	1.39920E-02	3.43133E-02
	MFRAC	6.09351E-02	2.78704E-05	2.78704E-05	2.78704E-05	2.78704E-05
	M/LH2O	0.	1.54692E-03	1.54692E-03	1.54692E-03	1.54692E-33
N2	MOLES	8.25800E 02	1.43041E-03	1.07089E-03	4.11403E-03	1.66340E-32
	MFRAC	8.25284E-01	8.19466E-06	1.35107E-05	8.19466E-06	1.35107E-35
	M/LH2O	0.	4.54836E-04	7.69898E-04	4.54836E-04	7.69898E-34
H2O	MOLES	6.11119E 01	1.73567E 02	7.88137E 01	4.99198E 02	1.22421E 03
	MFRAC	6.10738E-02	9.94343E-01	9.94343E-01	9.94343E-01	9.94343E-31
	M/LH2O	0.	5.51900E 01	5.51900E 01	5.51900E 01	5.51900E 01
H+	MOLES	-0.	1.15968E-07	8.32907E-08	3.18220E-07	3.04836E-36
	MFRAC	-0.	6.64367E-10	1.05032E-09	6.33055E-10	2.47598E-09
	M/LH2O	-0.	3.68750E-08	5.82970E-08	3.51815E-08	1.37427E-07
OH-	MOLES	-0.	2.04267E-06	5.86705E-07	6.15777E-06	3.86589E-06
	MFRAC	-0.	1.17022E-08	7.40209E-09	1.22655E-08	3.14000E-09
	M/LH2O	-0.	6.49520E-07	4.10845E-07	6.80786E-07	1.74283E-07
CL-	MOLES	-0.	3.17991E-01	9.13347E-02	9.58604E-01	8.14473E-32
	MFRAC	-0.	1.82173E-03	1.15231E-03	1.90942E-03	6.61542E-35
	M/LH2O	-0.	1.01113E-01	6.39579E-02	1.05981E-01	3.67182E-33
NA+	MOLES	-0.	4.71258E-01	3.91012E-02	1.29324E 00	2.24375E-01
	MFRAC	-0.	2.69978E-03	4.93316E-04	2.57598E-03	1.82245E-04
	M/LH2O	-0.	1.49848E-01	2.73810E-02	1.42977E-01	1.01153E-32
K+	MOLES	-0.	1.27893E-02	1.92616E-01	3.43729E-02	3.45892E 30
	MFRAC	-0.	7.32686E-05	2.42759E-03	6.84668E-05	2.80945E-03
	M/LH2O	-0.	4.06670E-03	1.34741E-01	3.80018E-03	1.55936E-01
CA++	MOLES	-0.	8.28622E-03	4.64867E-04	2.09581E-02	2.17355E-02
	MFRAC	-0.	4.74708E-05	5.86493E-06	4.17461E-05	1.76543E-05
	M/LH2O	-0.	2.63482E-03	3.25527E-04	2.31707E-03	9.79802E-04
MG++	MOLES	-0.	3.16166E-03	4.64902E-03	8.33154E-03	2.80818E-31
	MFRAC	-0.	1.81128E-05	5.86537E-05	1.65954E-05	2.28089E-34
	M/LH2O	-0.	1.00533E-03	3.25551E-03	9.21113E-04	1.26599E-32
SO4=	MOLES	-0.	1.63541E-03	2.97121E-04	5.16736E-03	2.19120E-31
	MFRAC	-0.	9.36906E-06	3.74858E-06	1.02928E-05	1.74728E-04
	M/LH2O	-0.	5.20020E-04	2.08061E-04	5.71289E-04	9.69808E-33
HPO4=	MOLES	-0.	3.39418E-03	6.16654E-04	1.07245E-02	1.07756E 00
	MFRAC	-0.	1.94448E-05	7.77993E-06	2.13619E-05	8.75234E-04
	M/LH2O	-0.	1.07927E-03	4.31817E-04	1.18567E-03	4.85789E-32
UREA	MOLES	-0.	1.11398E-02	5.05840E-03	3.20394E-02	7.85719E-32
	MFRAC	-0.	6.38187E-05	6.38187E-05	6.38187E-05	6.38187E-05
	M/LH2O	-0.	3.54219E-03	3.54219E-03	3.54219E-03	3.54219E-03
GLUCOS	MOLES	-0.	1.29969E-02	5.90167E-03	3.73806E-02	9.16703E-32
	MFRAC	-0.	7.44577E-05	7.44577E-05	7.44577E-05	7.44577E-35
	M/LH2O	-0.	4.13270E-03	4.13270E-03	4.13270E-03	4.13270E-33
LACTIC	MOLES	-0.	2.16215E-02	6.21022E-03	6.51796E-02	5.53796E-03
	MFRAC	-0.	1.23867E-04	7.83505E-05	1.29833E-04	4.49809E-36
	M/LH2O	-0.	6.87512E-03	4.34876E-03	7.20806E-03	2.49662E-04
HCO3-	MOLES	-0.	1.06544E-01	3.52007E-02	3.21183E-01	2.31943E-31
	MFRAC	-0.	6.10377E-04	4.44105E-04	6.39759E-04	1.88392E-34
	M/LH2O	-0.	3.38784E-02	2.44696E-02	3.55092E-02	1.04565E-02
H2CO3	MOLES	-0.	6.91800E-06	3.14134E-06	1.98970E-05	4.87943E-35
	MFRAC	-0.	3.96324E-08	3.96324E-08	3.96324E-08	3.96324E-08
	M/LH2O	-0.	2.19975E-06	2.19975E-06	2.19975E-06	2.19975E-06
CO3=	MOLES	-0.	1.63776E-04	3.42261E-05	5.17478E-04	9.56673E-05
	MFRAC	-0.	9.38252E-07	4.31810E-07	1.03076E-06	7.77041E-08
	M/LH2O	-0.	5.20767E-05	2.39671E-05	5.72110E-05	4.31289E-36
PROTN	MOLES	-0.	9.96000E-03	5.31130E-02	3.36030E-02	1.14374E 00
	MFRAC	-0.	5.70596E-05	6.70056E-04	6.69272E-05	9.28983E-04
	M/LH2O	-0.	3.16704E-03	3.71907E-02	3.71473E-03	5.15623E-02
HB4	MOLES	-0.	-0.	7.97823E-04	-0.	-0.
	MFRAC	-0.	-0.	1.00656E-05	-0.	-0.
	M/LH2O	-0.	-0.	5.58682E-04	-0.	-0.
HB4O2	MOLES	-0.	-0.	1.41529E-03	-0.	-0.
	MFRAC	-0.	-0.	1.78550E-05	-0.	-0.
	M/LH2O	-0.	-0.	9.91068E-04	-0.	-0.
HB4O4	MOLES	-0.	-0.	1.00384E-03	-0.	-0.
	MFRAC	-0.	-0.	1.26649E-05	-0.	-0.
	M/LH2O	-0.	-0.	7.02950E-04	-0.	-0.
HB4O6	MOLES	-0.	-0.	4.26364E-04	-0.	-0.
	MFRAC	-0.	-0.	5.37917E-06	-0.	-0.
	M/LH2O	-0.	-0.	2.98565E-04	-0.	-0.
HB4O8	MOLES	-0.	-0.	6.96668E-03	-0.	-0.
	MFRAC	-0.	-0.	8.78942E-05	-0.	-0.
	M/LH2O	-0.	-0.	4.87846E-03	-0.	-0.

intracellular Na^+ gradient changes with chemical stress. Obviously, this sort of data is difficult if not impossible to measure in vivo, and obtaining such data illustrates the usefulness of a computer model that has been verified and is reliable.

The global measurements for body water division, however, were illustrated in Fig. 3 for the computer and in vivo. One can conclude from Fig. 3 that the computer is qualitatively correct. Some of the quantitative differences can be attributed to the differences between man and dog, in particular to the reported difference in the sodium pump value. The red cell-plasma Na^+ ratio may be as low as 1:1 in the dog, whereas in man it is 7:1. We attribute the quantitative error in the predicted ECW to this difference. A mathematical dog model was not constructed because of a lack of sufficient data and because our primary goal was to consider human physiology.

WASTING DISEASE

Wasting disease, discussed in Moore [2, Chap. 5], is characterized by a loss of fat, a "skin-and'bones" appearance, and, particularly, by the predominance of extracellular tissues over intracellular, decreasing ICW/TBW

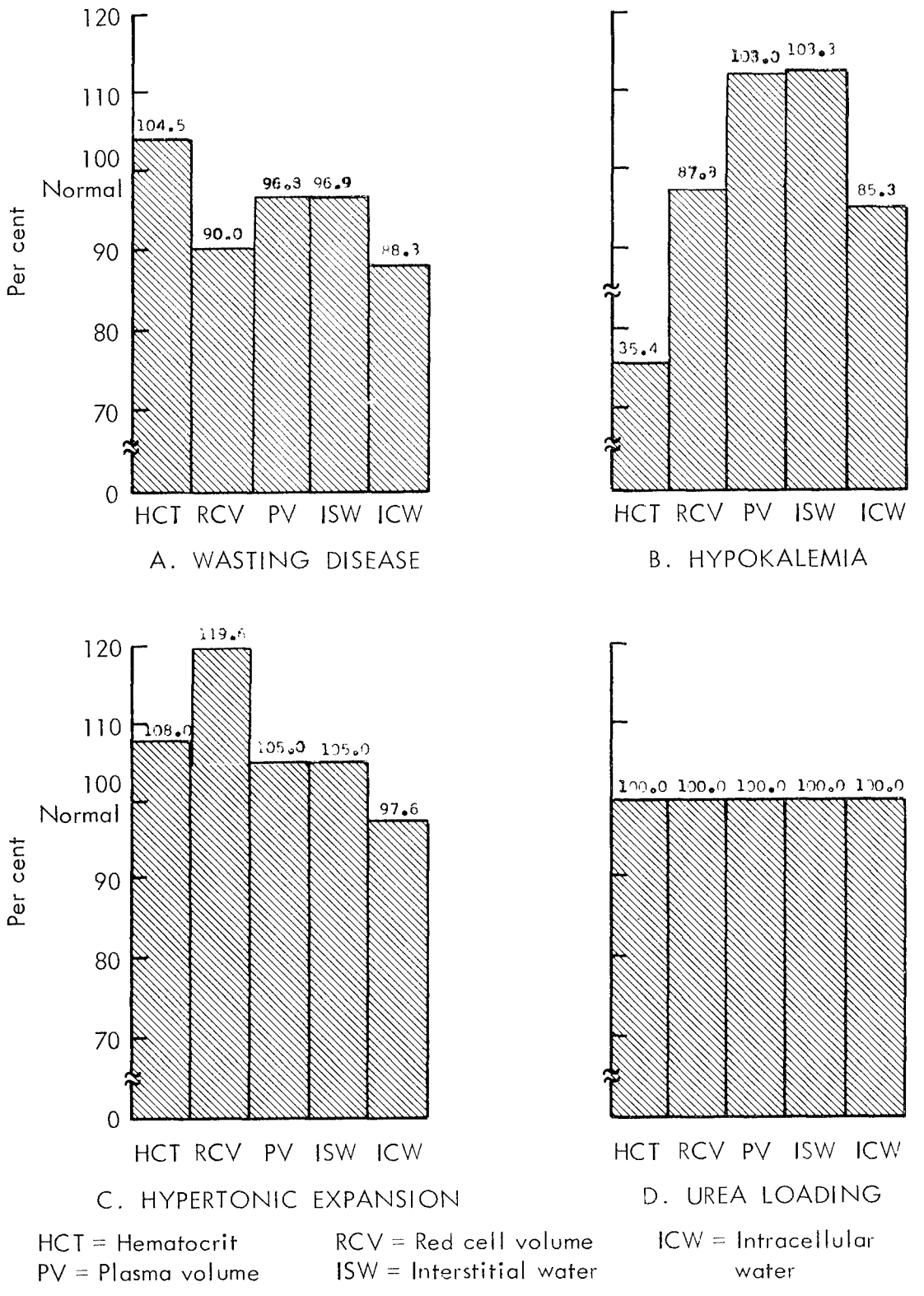
ratio, increasing Na_e/K_e, increasing Na^+ and Cl^- concentrations, and decreasing hematocrit. It occurs, for example, with cancer and in starvation.

We do not have enough data to check the computed results in detail, but it is perhaps surprising that the superficial characteristics of wasting disease can be simulated by simple loss of intracellular K^+ with a proportionate loss of intracellular water. Moore suggests that this is so, and his suggestion confirms the results of such a stress, shown in Fig. 4A and Table XVII. This test should be continued, particularly with, also, a loss of protein.

HYPOKALEMIA

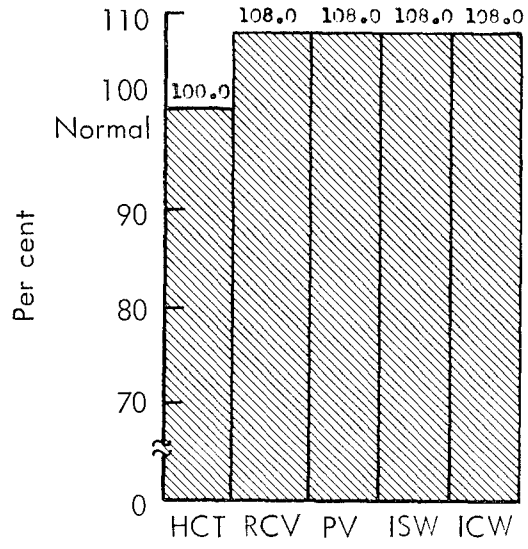
Hypokalemia, the loss of K^+, probably does not occur without water-loss from the cells [2] and we characterize it here (Fig. 4B and Table XVIII) by a loss of K^+ proportionately greater than the loss of intracellular water.

The computed results present an interesting comparison to wasting disease. In particular, "pitting edema" is a predominant characteristic where, as here, three liters of water carrying double the normal amount of intracellular K^+ are lost. Computed extracellular volumes actually go up in spite of the loss of water [2]. Hematocrit is, of course, very low. Plasma and interstitial Na^+ concentrations

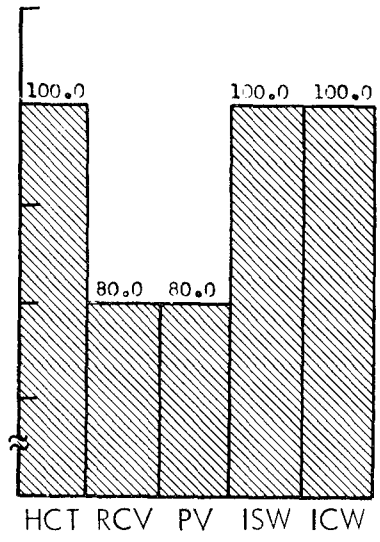


HCT = Hematocrit RCV = Red cell volume ICW = Intracellular water
PV = Plasma volume ISW = Interstitial water

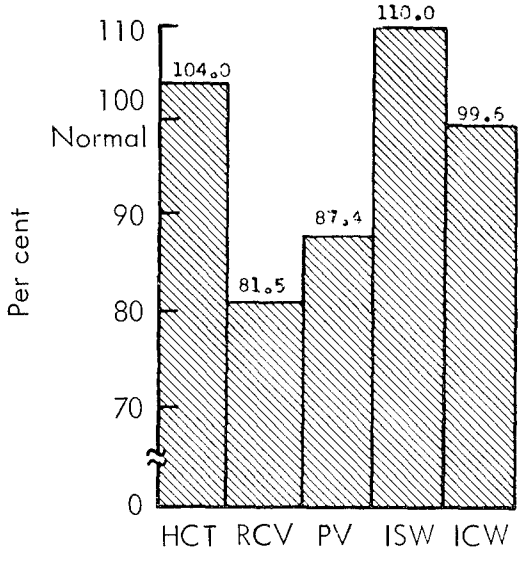
Fig. 4a—General tests (computed)



E. UREA PLUS H_2O LOADING



F. HEMORRHAGE



G. HEMORRHAGE PLUS ISOTONIC SALINE

HCT = Hematocrit
RCV = Red cell volume
PV = Plasma volume
ISW = Interstitial water
ICW = Intracellular water

Fig. 4b—General tests (computed)

Table XVII

WASTING DISEASE

TABLE XVII K+ LOSS PROPORTIONAL TO ICW LOSS (FIG. 4A)

		AIR	PLASMA	RED CELLS	INTERSTITIAL	INTRACELL
X-BAR		1.00061E 03	1.57564E 02	7.26799E 01	4.51419E 02	1.06185E 03
PH		-0.	7.40459E 00	7.20606E 00	7.42570E 00	6.85730E 00
O2	MOLES	5.27412E 01	1.47285E-04	7.13507E-05	4.21972E-04	1.62021E-03
	MFRAC	5.27090E-02	9.34767E-07	9.81712E-07	9.34767E-07	1.52584E-06
	M/LH2O	0.	5.19035E-05	5.45101E-05	5.19035E-05	8.47229E-05
CO2	MOLES	6.09789E 01	4.39183E-03	2.02584E-03	1.25826E-02	2.95974E-02
	MFRAC	6.09417E-02	2.78734E-05	2.78734E-05	2.78734E-05	2.78734E-05
	M/LH2O	0.	1.54769E-03	1.54769E-03	1.54769E-03	1.54769E-03
N2	MOLES	8.25802E 02	1.29120E-03	9.81975E-04	3.69929E-03	1.43466E-02
	MFRAC	8.25299E-01	8.19481E-06	1.35110E-05	8.19481E-06	1.35110E-05
	M/LH2O	0.	4.55022E-04	7.50204E-04	4.55022E-04	7.50204E-04
H2O	MOLES	6.10872E 01	1.56611E 02	7.22436E 01	4.48691E 02	1.05543E 03
	MFRAC	6.10500E-02	9.93956E-01	9.93956E-01	9.93956E-01	9.93956E-01
	M/LH2O	0.	5.51900E 01	5.51900E 01	5.51900E 01	5.51900E 01
H+	MOLES	-0.	1.11781E-07	8.14432E-08	3.05056E-07	2.65618E-06
	MFRAC	-0.	7.09434E-10	1.12057E-09	6.75772E-10	2.50147E-09
	M/LH2O	-0.	3.93917E-08	6.22205E-08	3.75227E-08	1.38895E-07
OH-	MOLES	-0.	1.72604E-06	5.04059E-07	5.19143E-06	3.29895E-06
	MFRAC	-0.	1.09546E-08	6.93533E-09	1.15002E-08	3.10680E-09
	M/LH2O	-0.	6.08259E-07	3.85088E-07	6.38558E-07	1.72507E-07
CL-	MOLES	-0.	3.17957E-01	9.28536E-02	9.56322E-01	8.22440E-02
	MFRAC	-0.	2.01796E-03	1.27757E-03	2.11848E-03	7.76535E-05
	M/LH2O	-0.	1.12049E-01	7.09378E-02	1.17630E-01	4.30065E-03
NA+	MOLES	-0.	4.52458E-01	3.81020E-02	1.23487E 00	1.94741E-01
	MFRAC	-0.	2.87159E-03	5.24264E-04	2.73554E-03	1.83398E-04
	M/LH2O	-0.	1.59447E-01	2.91089E-02	1.51892E-01	1.01833E-02
K+	MOLES	-0.	1.22222E-02	1.06630E-01	3.26695E-02	2.98817E 00
	MFRAC	-0.	7.75701E-05	2.56783E-03	7.23708E-05	2.81412E-03
	M/LH2O	-0.	4.30713E-03	1.42581E-01	4.01843E-03	1.56256E-01
CA++	MOLES	-0.	8.85174E-03	5.03561E-04	2.22308E-02	1.98586E-02
	MFRAC	-0.	5.61789E-05	6.92848E-06	4.92465E-05	1.87019E-05
	M/LH2O	-0.	3.11936E-03	3.84708E-04	2.73444E-03	1.03843E-03
MG++	MOLES	-0.	3.66286E-03	5.46158E-03	9.58432E-03	2.78251E-01
	MFRAC	-0.	2.32469E-05	7.51457E-05	2.12315E-05	2.62044E-04
	M/LH2O	-0.	1.29080E-03	4.17251E-03	1.17889E-03	1.45501E-02
SO4=	MOLES	-0.	1.53522E-03	2.83839E-04	4.84750E-03	2.15553E-01
	MFRAC	-0.	9.74350E-06	3.90533E-06	1.07384E-05	2.02998E-04
	M/LH2O	-0.	5.41014E-04	2.16846E-04	5.96254E-04	1.12716E-02
HPO4=	MOLES	-0.	3.18254E-03	5.88404E-04	1.00490E-02	1.07848E 00
	MFRAC	-0.	2.01985E-05	8.09582E-06	2.22608E-05	1.01566E-03
	M/LH2O	-0.	1.12153E-03	4.49525E-04	1.23605E-03	5.63952E-02
UREA	MOLES	-0.	1.14600E-02	5.28617E-03	3.28327E-02	7.72307E-02
	MFRAC	-0.	7.27323E-05	7.27323E-05	7.27323E-05	7.27323E-05
	M/LH2O	-0.	4.03850E-03	4.03850E-03	4.03850E-03	4.03850E-03
GLUCOS	MOLES	-0.	1.33704E-02	6.16741E-03	3.83061E-02	9.01056E-02
	MFRAC	-0.	8.48572E-05	8.48572E-05	8.48572E-05	8.48572E-05
	M/LH2O	-0.	4.71174E-03	4.71174E-03	4.71174E-03	4.71174E-03
LACTIC	MOLES	-0.	2.16192E-02	6.31350E-03	6.50243E-02	5.59211E-03
	MFRAC	-0.	1.37210E-04	8.58672E-05	1.44044E-04	5.26638E-06
	M/LH2O	-0.	7.61864E-03	4.82335E-03	7.99814E-03	2.92419E-04
HCO3-	MOLES	-0.	9.00386E-02	3.02454E-02	2.70810E-01	1.97949E-01
	MFRAC	-0.	5.71443E-04	4.16146E-04	5.99908E-04	1.86419E-04
	M/LH2O	-0.	3.17297E-02	2.31067E-02	3.33102E-02	1.03510E-02
H2CO3	MOLES	-0.	6.24287E-06	2.87967E-06	1.78858E-05	4.20718E-05
	MFRAC	-0.	3.96213E-08	3.96213E-08	3.96213E-08	3.96213E-08
	M/LH2O	-0.	2.19999E-06	2.19999E-06	2.19999E-06	2.19999E-06
CO3=	MOLES	-0.	1.29612E-04	2.75644E-05	4.09254E-04	8.08144E-05
	MFRAC	-0.	8.22603E-07	3.79258E-07	9.06595E-07	7.61072E-08
	M/LH2O	-0.	4.56755E-05	2.10585E-05	5.03392E-05	4.22589E-06
PROTN	MOLES	-0.	9.96000E-03	5.31130E-02	3.36030E-02	1.14374E 00
	MFRAC	-0.	6.32126E-05	7.30738E-04	7.44320E-05	1.07712E-03
	M/LH2O	-0.	3.50992E-03	4.05747E-02	4.13288E-03	5.98077E-02
HB4	MOLES	-0.	-0.	8.82460E-04	-0.	-0.
	MFRAC	-0.	-0.	1.21417E-05	-0.	-0.
	M/LH2O	-0.	-0.	6.74177E-04	-0.	-0.
HB402	MOLES	-0.	-0.	1.51431E-03	-0.	-0.
	MFRAC	-0.	-0.	2.08353E-05	-0.	-0.
	M/LH2O	-0.	-0.	1.15689E-03	-0.	-0.
HB404	MOLES	-0.	-0.	1.03900E-03	-0.	-0.
	MFRAC	-0.	-0.	1.42955E-05	-0.	-0.
	M/LH2O	-0.	-0.	7.93766E-04	-0.	-0.
HB406	MOLES	-0.	-0.	4.26882E-04	-0.	-0.
	MFRAC	-0.	-0.	5.87346E-06	-0.	-0.
	M/LH2O	-0.	-0.	3.26127E-04	-0.	-0.
HB408	MOLES	-0.	-0.	6.74736E-03	-0.	-0.
	MFRAC	-0.	-0.	9.28367E-05	-0.	-0.
	M/LH2O	-0.	-0.	5.15481E-03	-0.	-0.

Table XVIII

HYPOKALEMIA

TABLE XVIII K+ LOSS GREATER THAN ICW LOSS (FIG. 4B)

		AIR	PLASMA	RED CELLS	INTERSTITIAL	INTRACELL
X-BAR		1.00063E 03	1.67500E 02	7.08858E 01	4.80677E 02	1.02395E 03
PH		-0.	7.39159E 00	7.17616E 00	7.41234E 00	6.85704E 00
O2	MOLES	5.27420E 01	1.56574E-04	6.35893E-05	4.49320E-04	1.56238E-03
	MFRAC	5.27090E-02	9.34766E-07	9.81710E-07	9.34766E-07	1.52583E-06
	M/LH2O	0.	5.18892E-05	5.44951E-05	5.18892E-05	8.46996E-05
CO2	MOLES	6.09779E 01	4.66865E-03	1.97576E-03	1.33976E-02	2.85401E-02
	MFRAC	6.09396E-02	2.78724E-05	2.78724E-05	2.78724E-05	2.78724E-05
	M/LH2O	0.	1.54721E-03	1.54721E-03	1.54721E-03	1.54721E-03
N2	MOLES	8.25803E 02	1.37261E-03	9.57719E-04	3.93899E-03	1.38343E-02
	MFRAC	8.25285E-01	8.19467E-06	1.35107E-05	8.19467E-06	1.35107E-05
	M/LH2O	0.	4.54889E-04	7.49986E-04	4.54889E-04	7.49986E-04
H2O	MOLES	6.11050E 01	1.66534E 02	7.04767E 01	4.77902E 02	1.01804E 03
	MFRAC	6.10667E-02	9.94228E-01	9.94228E-01	9.94228E-01	9.94228E-01
	M/LH2O	0.	5.51900E 01	5.51900E 01	5.51900E 01	5.51900E 01
H+	MOLES	-0.	1.22475E-07	8.51174E-08	3.35065E-07	2.56362E-06
	MFRAC	-0.	7.31192E-10	1.20077E-09	6.97068E-10	2.50365E-09
	M/LH2O	-0.	4.05887E-08	6.66550E-08	3.86945E-08	1.38978E-07
OH-	MOLES	-0.	1.78078E-06	4.58910E-07	5.36049E-06	3.17931E-06
	MFRAC	-0.	1.06315E-08	6.47393E-09	1.11520E-08	3.10494E-09
	M/LH2O	-0.	5.90160E-07	3.59370E-07	6.19050E-07	1.72396E-07
CL-	MOLES	-0.	3.21405E-01	8.28264E-02	9.67488E-01	7.76578E-02
	MFRAC	-0.	1.91883E-03	1.16845E-03	2.01276E-03	7.58412E-05
	M/LH2O	-0.	1.06515E-01	6.48610E-02	1.11729E-01	4.20998E-03
NA+	MOLES	-0.	4.57681E-01	3.67634E-02	1.25221E 00	1.73523E-01
	MFRAC	-0.	2.73242E-03	5.18629E-04	2.60539E-03	1.69464E-04
	M/LH2O	-0.	1.51677E-01	2.87893E-02	1.44610E-01	9.40701E-03
K+	MOLES	-0.	1.17329E-02	1.70891E-01	3.14388E-02	2.52683E 00
	MFRAC	-0.	7.00468E-05	2.41079E-03	6.54053E-05	2.46772E-03
	M/LH2O	-0.	3.88833E-03	1.33824E-01	3.63067E-03	1.36984E-01
CA++	MOLES	-0.	9.36173E-03	5.28156E-04	2.35888E-02	1.79660E-02
	MFRAC	-0.	5.58908E-05	7.45080E-06	4.90742E-05	1.75457E-05
	M/LH2O	-0.	3.10252E-03	4.13597E-04	2.72413E-03	9.73969E-04
MG++	MOLES	-0.	4.23710E-03	6.26541E-03	1.11233E-02	2.75334E-01
	MFRAC	-0.	2.52961E-05	8.83873E-05	2.31409E-05	2.68893E-04
	M/LH2O	-0.	1.40419E-03	4.90641E-03	1.28456E-03	1.49266E-02
SO4=	MOLES	-0.	1.59463E-03	2.50203E-04	5.03467E-03	2.15341E-01
	MFRAC	-0.	9.51893E-06	3.52966E-06	1.04737E-05	2.10304E-04
	M/LH2O	-0.	5.28399E-04	1.95933E-04	5.81399E-04	1.16740E-02
HPO4=	MOLES	-0.	3.30716E-03	5.18972E-04	1.04425E-02	1.07803E 00
	MFRAC	-0.	1.97442E-05	7.32124E-06	2.17246E-05	1.05281E-03
	M/LH2O	-0.	1.09601E-03	4.36435E-04	1.20594E-03	5.84421E-02
UREA	MOLES	-0.	1.21862E-02	5.15716E-03	3.49707E-02	7.44956E-02
	MFRAC	-0.	7.27530E-05	7.27530E-05	7.27530E-05	7.27530E-05
	M/LH2O	-0.	4.03855E-03	4.03855E-03	4.03855E-03	4.03855E-03
GLUCOS	MOLES	-0.	1.42177E-02	6.01689E-03	4.08005E-02	8.69145E-02
	MFRAC	-0.	8.48814E-05	8.48814E-05	8.48814E-05	8.48814E-05
	M/LH2O	-0.	4.71180E-03	4.71180E-03	4.71180E-03	4.71180E-03
LACTIC	MOLES	-0.	2.18536E-02	5.63170E-03	6.57835E-02	5.28027E-03
	MFRAC	-0.	1.30469E-04	7.94475E-05	1.36856E-04	5.15676E-06
	M/LH2O	-0.	7.24239E-03	4.41016E-03	7.59693E-03	2.86256E-04
HCO3-	MOLES	-0.	9.28910E-02	2.75354E-02	2.79619E-01	1.90764E-01
	MFRAC	-0.	5.54571E-04	3.88467E-04	5.81719E-04	1.86302E-04
	M/LH2O	-0.	3.07845E-02	2.15628E-02	3.22915E-02	1.03417E-02
H2CO3	MOLES	-0.	6.63817E-06	2.80926E-06	1.90496E-05	4.05800E-05
	MFRAC	-0.	3.96308E-08	3.96308E-08	3.96308E-08	3.96308E-08
	M/LH2O	-0.	2.19992E-06	2.19992E-06	2.19992E-06	2.19992E-06
CO3=	MOLES	-0.	1.29739E-04	2.34186E-05	4.09657E-04	7.78131E-03
	MFRAC	-0.	7.74561E-07	3.30371E-07	8.52251E-07	7.59929E-08
	M/LH2O	-0.	4.29962E-05	1.83390E-05	4.73088E-05	4.21839E-06
PROTN	MOLES	-0.	9.96000E-03	5.31100E-02	3.36000E-02	1.14374E 00
	MFRAC	-0.	5.94625E-05	7.49233E-04	6.99015E-05	1.11699E-03
	M/LH2O	-0.	3.30079E-03	4.15902E-02	3.88026E-03	6.20043E-02
HB4	MOLES	-0.	-0.	9.34967E-04	-0.	-0.
	MFRAC	-0.	-0.	1.38951E-05	-0.	-0.
	M/LH2O	-0.	-0.	7.71323E-04	-0.	-0.
HB4O2	MOLES	-0.	-0.	1.52869E-03	-0.	-0.
	MFRAC	-0.	-0.	2.29763E-05	-0.	-0.
	M/LH2O	-0.	-0.	1.27542E-03	-0.	-0.
HB4O4	MOLES	-0.	-0.	1.07681E-03	-0.	-0.
	MFRAC	-0.	-0.	1.51938E-05	-0.	-0.
	M/LH2O	-0.	-0.	8.43247E-04	-0.	-0.
HB4O6	MOLES	-0.	-0.	4.26318E-04	-0.	-0.
	MFRAC	-0.	-0.	6.01415E-06	-0.	-0.
	M/LH2O	-0.	-0.	3.33848E-04	-0.	-0.
HB4O8	MOLES	-0.	-0.	6.49371E-03	-0.	-0.
	MFRAC	-0.	-0.	9.16009E-05	-0.	-0.
	M/LH2O	-0.	-0.	5.08480E-03	-0.	-0.

remain almost normal, while intracellular Na^+ goes up, pH is changed slightly toward alkalosis, and intracellular Cl^- and HCO_3^- increase. These results require laboratory confirmation.

HYPERTONIC EXPANSION

Hypertonic expansion of body fluids occurs after stressing the system with a hypertonic salt solution [28]. The specific effects of the hypertonic solution, however, depend greatly upon the kind of salts infused.

Bland [28] discusses hypertonic expansion due to the infusion of saline, and in the computed experiment of Fig. 3C, Table XIII above, the principal result, cellular dehydration, confirms Bland's remarks. The ingestion of sea water, though principally saline, gives somewhat different results [29], and the present experiment in which both Na^+ and K^+ are infused at hypertonic strength, gives still different results.

In the present case, the infusion is 5 ml/kg of 0.408 M NaCl, plus 5 ml/kg of 0.408 M KCl (each alone would be hypertonic), with the result shown in Fig. 4C and Table XIX. (A similar mixture is deducted from the system in Table XX.)

The effects on the fluid and electrolyte distribution of adding Na^+ and K^+ are not exactly the algebraic sum of the two effects of the stresses added separately, but, for small stresses, the qualitative results for mixed stresses can be predicted by such addition. Generally, for example, from the computer, hypertonic saline infusion will dehydrate the cells while hypertonic potassium infusion will transfer water from extracellular to intracellular spaces.

With the present mixed infusion, the computed extracellular volume goes up by 5 per cent and red cell volume by 19 per cent, but muscle tissue volume decreases 3 per cent, a mixed effect. Both Na^+ and K^+ have shifted out of the cells, the concentration gradient for Na^+ increasing and for K^+ (into the cell) decreasing. The pH intracellularly remains constant but the extracellular pH is more acidic. The hematocrit rises slightly under the influence of this stress to 42; the hemoglobin saturation is 75 per cent.

The behavior of the Cl^- ion here is of special interest since often the Cl^- ion is presumed to be the ion which moves along with Na^+ in order to maintain charge neutrality. In fact, the concentration of Cl^- increases in all compartments, and, further, there is a preferential rise in Cl^- intracellularly although the Na^+ tends to accumulate

Table XIX

HYPERTONIC EXPANSION

TABLE XIX 5ML/KG OF 0.408 M NACL PLUS 0.408 M KCL (FIG. 4C)

		AIR	PLASMA	RED CELLS	INTERSTITIAL	INTRACELL
X-BAR		1.00061E 03	1.70546E 02	9.65555E 01	4.89128E 02	1.17308E 03
PH		-0.	7.34848E 00	7.20820E 00	7.36831E 00	6.83137E 00
O2	MOLES	5.27409E 01	1.59420E-04	9.47893E-05	4.57219E-04	1.78992E-03
	MFRAC	5.27088E-02	9.34763E-07	9.31737E-07	9.34763E-07	1.52583E-06
	M/LH2O	0.	5.18977E-05	5.45040E-05	5.18977E-05	8.47135E-05
CO2	MOLES	6.09737E 01	4.75329E-03	2.69110E-03	1.36325E-02	3.26950E-02
	MFRAC	6.09366E-02	2.78711E-05	2.78711E-05	2.78711E-05	2.78711E-05
	M/LH2O	0.	1.54739E-03	1.54739E-03	1.54739E-03	1.54739E-03
N2	MOLES	8.25800E 02	1.39759E-03	1.30456E-03	4.00831E-03	1.58494E-02
	MFRAC	8.25298E-01	8.19480E-06	1.35109E-05	8.19480E-06	1.35109E-05
	M/LH2O	0.	4.54972E-04	7.50122E-04	4.54972E-04	7.50122E-04
H2O	MOLES	6.10937E 01	1.69533E 02	9.59823E 01	4.86224E 02	1.16612E 03
	MFRAC	6.10566E-02	9.94063E-01	9.94063E-01	9.94063E-01	9.94063E-01
	M/LH2O	0.	5.51900E 01	5.51900E 01	5.51900E 01	5.51900E 01
H+	MOLES	-0.	1.37690E-07	1.37676E-07	3.77273E-07	3.11535E-06
	MFRAC	-0.	8.07351E-10	1.11518E-09	7.71316E-10	2.65570E-09
	M/LH2O	-0.	4.48238E-08	6.19142E-08	4.28232E-08	1.47444E-07
OH-	MOLES	-0.	1.64185E-06	6.72957E-07	4.92884E-06	3.43323E-06
	MFRAC	-0.	9.62701E-09	6.96964E-09	1.00768E-08	2.92668E-09
	M/LH2O	-0.	5.34488E-07	3.86952E-07	5.59459E-07	1.62488E-07
CL-	MOLES	-0.	3.54637E-01	1.45358E-01	1.06462E 00	1.00361E-01
	MFRAC	-0.	2.07942E-03	1.50543E-03	2.17657E-03	8.55533E-05
	M/LH2O	-0.	1.15449E-01	8.35811E-02	1.20842E-01	4.74989E-03
NA+	MOLES	-0.	4.78249E-01	4.32268E-02	1.31050E 00	1.95996E-01
	MFRAC	-0.	2.80422E-03	4.47689E-04	2.67926E-03	1.67078E-04
	M/LH2O	-0.	1.55690E-01	2.48555E-02	1.48752E-01	9.27609E-03
K+	MOLES	-0.	1.50527E-02	2.46703E-01	4.03967E-02	3.50415E 00
	MFRAC	-0.	8.82618E-05	2.55504E-03	8.25831E-05	2.98713E-03
	M/LH2O	-0.	4.90026E-03	1.41855E-01	4.58532E-03	1.65845E-01
CA++	MOLES	-0.	9.22741E-03	4.92704E-04	2.33360E-02	1.83885E-02
	MFRAC	-0.	5.41052E-05	5.10280E-06	4.77095E-05	1.56754E-05
	M/LH2O	-0.	3.00390E-03	2.83306E-04	2.64881E-03	8.70293E-04
MG++	MOLES	-0.	4.09528E-03	5.73145E-03	1.07936E-02	2.76343E-01
	MFRAC	-0.	2.40128E-05	5.93591E-05	2.20609E-05	2.35570E-04
	M/LH2O	-0.	1.33318E-03	3.29560E-03	1.22481E-03	1.30788E-02
SO4=	MOLES	-0.	1.31412E-03	3.89949E-04	4.12933E-03	2.16387E-01
	MFRAC	-0.	7.70536E-06	4.03860E-06	8.44215E-06	1.84460E-04
	M/LH2O	-0.	4.27799E-04	2.24222E-04	4.68705E-04	1.02412E-02
HPO4=	MOLES	-0.	2.71812E-03	8.06570E-04	8.54102E-03	1.08023E 00
	MFRAC	-0.	1.59377E-05	8.35343E-06	1.74617E-05	9.20853E-04
	M/LH2O	-0.	8.84858E-04	4.63779E-04	9.69468E-04	5.11254E-02
UREA	MOLES	-0.	1.12096E-02	6.34640E-03	3.21494E-02	7.71042E-02
	MFRAC	-0.	6.57279E-05	6.57279E-05	6.57279E-05	6.57279E-05
	M/LH2O	-0.	3.64919E-03	3.64919E-03	3.64919E-03	3.64919E-03
GLUCOS	MOLES	-0.	1.30783E-02	7.40438E-03	3.75089E-02	8.99579E-02
	MFRAC	-0.	7.66852E-05	7.66852E-05	7.66852E-05	7.66852E-05
	M/LH2O	-0.	4.25753E-03	4.25753E-03	4.25753E-03	4.25753E-03
LACTIC	MOLES	-0.	2.09908E-02	8.50366E-03	6.30144E-02	5.94031E-03
	MFRAC	-0.	1.23080E-04	8.31058E-05	1.28830E-04	5.06386E-06
	M/LH2O	-0.	6.83335E-03	4.94712E-03	7.15257E-03	2.81143E-04
HCO3-	MOLES	-0.	8.56393E-02	4.03766E-02	2.57093E-01	2.05989E-01
	MFRAC	-0.	5.02149E-04	4.18170E-04	5.25608E-04	1.75597E-04
	M/LH2O	-0.	2.78791E-02	2.32166E-02	2.91816E-02	9.74908E-03
H2CO3	MOLES	-0.	6.75740E-06	3.82574E-06	1.93803E-05	4.64800E-05
	MFRAC	-0.	3.96222E-08	3.96222E-08	3.96222E-08	3.96222E-08
	M/LH2O	-0.	2.19981E-06	2.19981E-06	2.19981E-06	2.19981E-06
CO3=	MOLES	-0.	1.08328E-04	3.69756E-05	3.40394E-04	7.92127E-05
	MFRAC	-0.	6.35183E-07	3.82946E-07	6.95919E-07	6.75254E-08
	M/LH2O	-0.	3.52651E-05	2.12611E-05	3.86372E-05	3.74898E-06
PROTN	MOLES	-0.	9.96000E-03	5.31100E-02	3.36000E-02	1.14374E 00
	MFRAC	-0.	5.84007E-05	5.50046E-04	6.86936E-05	9.74988E-04
	M/LH2O	-0.	3.24239E-03	3.05384E-02	3.81385E-03	5.41310E-02
HB4	MOLES	-0.	-0.	8.75785E-04	-0.	-0.
	MFRAC	-0.	-0.	9.07028E-06	-0.	-0.
	M/LH2O	-0.	-0.	5.03578E-04	-0.	-0.
HB402	MOLES	-0.	-0.	1.50665E-03	-0.	-0.
	MFRAC	-0.	-0.	1.56040E-05	-0.	-0.
	M/LH2O	-0.	-0.	8.66328E-04	-0.	-0.
HB404	MOLES	-0.	-0.	1.33636E-03	-0.	-0.
	MFRAC	-0.	-0.	1.37333E-05	-0.	-0.
	M/LH2O	-0.	-0.	5.95910E-04	-0.	-0.
HB406	MOLES	-0.	-0.	4.26876E-04	-0.	-0.
	MFRAC	-0.	-0.	4.42135E-06	-0.	-0.
	M/LH2O	-0.	-0.	2.45455E-04	-0.	-0.
HB408	MOLES	-0.	-0.	6.76433E-03	-0.	-0.
	MFRAC	-0.	-0.	7.00564E-05	-0.	-0.
	M/LH2O	-0.	-0.	3.88951E-03	-0.	-0.

extracellularly. The difference in behavior of these ions is due to the preferential nature of the Na^+ pump, which affects the Cl^- only indirectly. In addition, the computed HCO_3^- ion concentration decreases extracellularly and increases intracellularly. Yet, in all of these shifts the requirements of charge neutrality and Gibbs-Donnan are satisfied. This example illustrates that the prediction of electrolyte shifts under even simple stress can be an intricate process.

Hypotonic contraction occurs when a hypertonic solution is lost from the system [28, Chap. 8]. The computed result of such a loss is shown in Table XX where just the reverse of the hypertonic expansion occurs.

An interesting conjecture coming from these experiments is that a physician, with sufficiently detailed knowledge of this sort, could tailor infusions of the proper salts to produce just the resulting electrolyte and fluid shifts desired.

UREA LOAD, WATER LOAD--FIRST APPROXIMATION TO RENAL FAILURE

In Figs. 4D and 4E, Tables XXI and XXII, we have made a rudimentary simulation of renal failure in a first attempt to simulate the syndrome. The first type of failure is a renal insufficiency where there is an accumulation of urea and

Table XX

HYPOTONIC CONTRACTION

TABLE XX DEDUCT 5ML/KG OF 3.408 % NACL PLUS 0.408 M KCL

		AIR	PLASMA	RED CELLS	INTERSTITIAL	INTRACELL
X-BAR		1.00063E 03	1.53540E 02	6.92588E 01	4.37434E 02	1.22959E 03
PH		-0.	7.41352E 00	7.18143E 00	7.43702E 00	6.80762E 00
O2	MOLES	5.27416E 01	1.43522E-04	6.79912E-05	4.08866E-04	1.87612E-03
	MFRAC	5.27083E-02	9.34755E-07	9.81698E-07	9.34755E-07	1.52582E-06
	M/LH2O	0.	5.18799E-05	5.44853E-05	5.18799E-05	8.46844E-05
CO2	MOLES	6.09739E 01	4.27924E-03	1.93078E-03	1.21907E-02	3.42693E-02
	MFRAC	6.09355E-02	2.78705E-05	2.78705E-05	2.78705E-05	2.78705E-05
	M/LH2O	0.	1.54685E-03	1.54685E-03	1.54685E-03	1.54685E-03
N2	MOLES	8.25800E 02	1.25820E-03	9.35730E-04	3.58436E-03	1.66125E-02
	MFRAC	8.25279E-01	8.19461E-06	1.35106E-05	8.19461E-06	1.35106E-05
	M/LH2O	0.	4.54810E-04	7.49855E-04	4.54810E-04	7.49855E-04
H2O	MOLES	6.11155E 01	1.52679E 02	6.98725E 01	4.34953E 02	1.22270E 03
	MFRAC	6.10769E-02	9.94395E-01	9.94395E-01	9.94395E-01	9.94395E-01
	M/LH2O	0.	5.51900E 01	5.51900E 01	5.51900E 01	5.51900E 01
H+	MOLES	-0.	1.06756E-07	8.21748E-08	2.88109E-07	3.45011E-06
	MFRAC	-0.	6.95295E-10	1.18649E-09	6.58680E-10	2.80591E-09
	M/LH2O	-0.	3.85896E-08	6.58515E-08	3.65574E-08	1.55731E-07
OH-	MOLES	-0.	1.71693E-06	4.53048E-07	5.16307E-06	3.40710E-06
	MFRAC	-0.	1.11823E-08	6.55293E-09	1.18039E-08	2.77093E-09
	M/LH2O	-0.	6.20629E-07	3.63695E-07	6.55129E-07	1.53790E-07
CL-	MOLES	-0.	2.71754E-01	7.18346E-02	8.17206E-01	7.29827E-02
	MFRAC	-0.	1.76992E-03	1.03719E-03	1.86831E-03	5.93554E-05
	M/LH2O	-0.	9.82326E-02	5.75653E-02	1.03693E-01	3.29429E-03
NA+	MOLES	-0.	4.14416E-01	3.68695E-02	1.11850E 00	2.42588E-01
	MFRAC	-0.	2.69908E-03	5.32344E-04	2.55713E-03	1.97292E-04
	M/LH2O	-0.	1.49802E-01	2.95457E-02	1.41923E-01	1.09499E-02
K+	MOLES	-0.	1.01925E-02	1.64427E-01	2.69619E-02	3.38914E 00
	MFRAC	-0.	6.63834E-05	2.37410E-03	6.15950E-05	2.75632E-03
	M/LH2O	-0.	3.68435E-03	1.31765E-01	3.41859E-03	1.52979E-01
CA++	MOLES	-0.	7.32090E-03	4.75352E-04	1.80827E-02	2.55658E-02
	MFRAC	-0.	4.76807E-05	6.96342E-06	4.13439E-05	2.07921E-05
	M/LH2O	-0.	2.64633E-03	3.80928E-04	2.29446E-03	1.15399E-03
MG++	MOLES	-0.	2.40409E-03	4.39145E-03	6.18678E-03	2.84278E-01
	MFRAC	-0.	1.56578E-05	5.93748E-05	1.41443E-05	2.31197E-04
	M/LH2O	-0.	8.69024E-04	3.27872E-03	7.85024E-04	1.28317E-02
SO4=	MOLES	-0.	1.68731E-03	2.61372E-04	5.35607E-03	2.14915E-01
	MFRAC	-0.	1.09894E-05	3.77385E-06	1.22451E-05	1.74786E-04
	M/LH2O	-0.	6.09924E-04	2.09453E-04	5.79618E-04	9.70083E-03
HPO4=	MOLES	-0.	3.50383E-03	5.42759E-04	1.11223E-02	1.07713E 00
	MFRAC	-0.	2.28203E-05	7.83668E-06	2.54279E-05	8.76010E-04
	M/LH2O	-0.	1.26655E-03	4.34944E-04	1.41128E-03	4.86195E-02
UREA	MOLES	-0.	1.03029E-02	4.54743E-03	2.93539E-02	8.25083E-02
	MFRAC	-0.	6.71024E-05	6.71024E-05	6.71024E-05	6.71024E-05
	M/LH2O	-0.	3.72426E-03	3.72426E-03	3.72426E-03	3.72426E-03
GLUCOS	MOLES	-0.	1.20205E-02	5.42219E-03	3.42439E-02	9.62630E-02
	MFRAC	-0.	7.82888E-05	7.82888E-05	7.82888E-05	7.82888E-05
	M/LH2O	-0.	4.34511E-03	4.34511E-03	4.34511E-03	4.34511E-03
LACTIC	MOLES	-0.	2.17066E-02	5.73786E-03	6.52751E-02	5.82955E-03
	MFRAC	-0.	1.41374E-04	8.28667E-05	1.49233E-04	4.74107E-06
	M/LH2O	-0.	7.84642E-03	4.59808E-03	8.28259E-03	2.63135E-04
HCO3-	MOLES	-0.	8.95539E-02	2.72298E-02	2.69303E-01	2.04418E-01
	MFRAC	-0.	5.83261E-04	3.93160E-04	6.15684E-04	1.66249E-04
	M/LH2O	-0.	3.23716E-02	2.18208E-02	3.41711E-02	9.22702E-03
H2CO3	MOLES	-0.	6.08551E-06	2.74505E-06	1.73364E-05	4.87343E-05
	MFRAC	-0.	3.96347E-08	3.96347E-08	3.96347E-08	3.96347E-08
	M/LH2O	-0.	2.19977E-06	2.19977E-06	2.19977E-06	2.19977E-06
CO3=	MOLES	-0.	1.31538E-04	2.34374E-05	4.17538E-04	7.44004E-05
	MFRAC	-0.	8.56690E-07	3.38404E-07	9.54581E-07	6.05084E-08
	M/LH2O	-0.	4.75472E-05	1.87818E-05	5.29803E-05	3.35828E-06
PROTN	MOLES	-0.	9.96000E-03	5.31130E-02	3.36033E-02	1.14374E 00
	MFRAC	-0.	6.48691E-05	7.66834E-04	7.68168E-05	9.30181E-04
	M/LH2O	-0.	3.60031E-03	4.25602E-02	4.26342E-03	5.16261E-02
HB4	MOLES	-0.	-0.	9.56347E-04	-0.	-0.
	MFRAC	-0.	-0.	1.39527E-05	-0.	-0.
	M/LH2O	-0.	-0.	7.74391E-04	-0.	-0.
HB4O2	MOLES	-0.	-0.	1.60834E-03	-0.	-0.
	MFRAC	-0.	-0.	2.32222E-05	-0.	-0.
	M/LH2O	-0.	-0.	1.28886E-03	-0.	-0.
HB4O4	MOLES	-0.	-0.	1.37030E-03	-0.	-0.
	MFRAC	-0.	-0.	1.54536E-05	-0.	-0.
	M/LH2O	-0.	-0.	8.57694E-04	-0.	-0.
HB4O6	MOLES	-0.	-0.	4.26507E-04	-0.	-0.
	MFRAC	-0.	-0.	6.15817E-06	-0.	-0.
	M/LH2O	-0.	-0.	3.41785E-04	-0.	-0.
HB4O8	MOLES	-0.	-0.	6.53851E-03	-0.	-0.
	MFRAC	-0.	-0.	9.44069E-05	-0.	-0.
	M/LH2O	-0.	-0.	5.23969E-03	-0.	-0.

water. These tests were made to demonstrate that the accumulation of urea or water *per se* does *not* account for the marked changes in body fluid and electrolytes reported, for example, in Remenchik, *et al*. [31], where renal insufficiency is discussed, or in Moore [2] and Bland [29] where renal failure in particular is analyzed.

The computed changes to be noted here, in urea and water accumulation, are not remarkable in any way. Both urea and water simply distribute uniformly in all compartments. The results for urea plus water accumulation are similar in every way to overhydration, as discussed above, including the fall of pH.

On the other hand, if K^+ is lost simultaneously with water loading, some of the general characteristics of uremia appear, and no doubt the symptoms would be exaggerated by loss of phosphate and calcium, as Moore points out [2, Chap. 10]. The addition of sodium salts as well would contribute to generalized acidosis (Table XIII), but perhaps, as Moore suggests, the accumulation of H^+ ions from metabolic sources may be the ultimately lethal change. The results from the computer are, of course, very tentative, and we only suggest here some preliminary results for a later concerted research of uremia with a laboratory.

Table XXI

UREA LOADING--APPROXIMATION TO RENAL FAILURE

TABLE XXI QUADRUPLE UREA CONTENT (FIG. 6D)

		AIR	PLASMA	RED CELLS	INTERSTITIAL	INTRACELL
X-BAR		1.00060E 03	1.62700E 02	8.06872E 01	4.65429E 02	1.20126E 03
PH		-0.	7.37860E 00	7.19594E 00	7.40036E 00	6.82141E 00
O2	MOLES	5.27412E 01	1.52088E-04	7.32122E-05	4.35072E-04	1.83294E-03
	MFRAC	5.27095E-02	9.34775E-07	9.81719E-07	9.34775E-07	1.52585E-06
	M/LH2O	0.	5.19036E-05	5.45102E-05	5.19036E-05	8.47230E-05
CO2	MOLES	6.09738E 01	4.53467E-03	2.24886E-03	1.29721E-02	3.34806E-02
	MFRAC	6.09371E-02	2.78713E-05	2.78713E-05	2.78713E-05	2.78713E-05
	M/LH2O	0.	1.54756E-03	1.54756E-03	1.54756E-03	1.54756E-03
N2	MOLES	8.25800E 02	1.33330E-03	1.09017E-03	3.81412E-03	1.62302E-02
	MFRAC	8.25303E-01	8.19485E-06	1.35110E-05	8.19485E-06	1.35110E-05
	M/LH2O	0.	4.55021E-04	7.50202E-04	4.55021E-04	7.50202E-04
H2O	MOLES	6.10872E 01	1.61718E 02	8.02001E 01	4.62620E 02	1.19401E 03
	MFRAC	6.10504E-02	9.93963E-01	9.93963E-01	9.93963E-01	9.93963E-01
	M/LH2O	0.	5.51900E 01	5.51930E 01	5.51900E 01	5.51900E 01
H+	MOLES	-0.	1.22543E-07	9.25480E-08	3.33654E-07	3.26387E-06
	MFRAC	-0.	7.53184E-10	1.14700E-09	7.16872E-10	2.71705E-09
	M/LH2O	-0.	4.18207E-08	6.36872E-08	3.98045E-08	1.50865E-07
OH-	MOLES	-0.	1.67879E-06	5.46736E-07	5.04571E-06	3.43597E-06
	MFRAC	-0.	1.03183E-08	6.77561E-09	1.08410E-08	2.86031E-09
	M/LH2O	-0.	5.72928E-07	3.76217E-07	6.01948E-07	1.58819E-07
CL-	MOLES	-0.	3.14521E-01	1.02425E-01	9.45312E-01	8.71191E-02
	MFRAC	-0.	1.93313E-03	1.26941E-03	2.03105E-03	7.25232E-05
	M/LH2O	-0.	1.07338E-01	7.04841E-02	1.12775E-01	4.02687E-03
NA+	MOLES	-0.	4.47319E-01	3.90458E-02	1.21801E 00	2.15798E-01
	MFRAC	-0.	2.74932E-03	4.83915E-04	2.61697E-03	1.79643E-04
	M/LH2O	-0.	1.52657E-01	2.68695E-02	1.45308E-01	9.97472E-03
K+	MOLES	-0.	1.26000E-02	1.99431E-01	3.36014E-02	3.45287E 00
	MFRAC	-0.	7.74430E-05	2.47165E-03	7.21944E-05	2.87438E-03
	M/LH2O	-0.	4.30004E-03	1.37239E-01	4.00861E-03	1.59600E-01
CA++	MOLES	-0.	8.38792E-03	4.76871E-04	2.10004E-02	2.15795E-02
	MFRAC	-0.	5.15545E-05	5.91012E-06	4.51205E-05	1.79641E-05
	M/LH2O	-0.	2.86257E-03	3.28161E-04	2.50532E-03	9.97460E-04
MG++	MOLES	-0.	3.22041E-03	4.79880E-03	8.40038E-03	2.80540E-01
	MFRAC	-0.	1.97935E-05	5.94741E-05	1.80487E-05	2.33539E-04
	M/LH2O	-0.	1.09904E-03	3.30231E-03	1.00216E-03	1.29673E-02
SO4=	MOLES	-0.	1.46843E-03	3.14013E-04	4.63701E-03	2.15800E-01
	MFRAC	-0.	9.02538E-06	3.89174E-06	9.96286E-06	1.79645E-04
	M/LH2O	-0.	5.01136E-04	2.16089E-04	5.53190E-04	9.97485E-03
HPO4=	MOLES	-0.	3.04207E-03	6.50525E-04	9.60624E-03	1.07900E 00
	MFRAC	-0.	1.86974E-05	8.06230E-06	2.06395E-05	8.98226E-04
	M/LH2O	-0.	1.03818E-03	4.47661E-04	1.14601E-03	4.98742E-02
UREA	MOLES	-0.	5.40083E-02	2.67841E-02	1.54499E-01	3.98758E-01
	MFRAC	-0.	3.31950E-04	3.31950E-04	3.31950E-04	3.31950E-04
	M/LH2O	-0.	1.84316E-02	1.84316E-02	1.84316E-02	1.84316E-02
GLUCOS	MOLES	-0.	1.26023E-02	6.26983E-03	3.60510E-02	9.30464E-02
	MFRAC	-0.	7.74574E-05	7.74574E-05	7.74574E-05	7.74574E-05
	M/LH2O	-0.	4.30084E-03	4.30084E-03	4.30084E-03	4.30084E-03
LACTIC	MOLES	-0.	2.13856E-02	6.96430E-03	6.42756E-02	5.92359E-03
	MFRAC	-0.	1.31442E-04	8.63122E-05	1.38100E-04	4.93115E-06
	M/LH2O	-0.	7.29833E-03	4.79250E-03	7.66801E-03	2.73803E-04
HCO3-	MOLES	-0.	8.75673E-02	3.28019E-02	2.63189E-01	2.06156E-01
	MFRAC	-0.	5.38213E-04	4.06532E-04	5.65475E-04	1.71617E-04
	M/LH2O	-0.	2.98844E-02	2.25728E-02	3.13981E-02	9.52905E-03
H2CO3	MOLES	-0.	6.44595E-06	3.19671E-06	1.84397E-05	4.75921E-05
	MFRAC	-0.	3.96186E-08	3.96186E-08	3.96186E-08	3.96186E-08
	M/LH2O	-0.	2.19983E-06	2.19983E-06	2.19983E-06	2.19983E-06
CO3=	MOLES	-0.	1.18733E-04	2.92056E-05	3.74934E-04	7.74869E-05
	MFRAC	-0.	7.29764E-07	3.61961E-07	8.05566E-07	6.45048E-08
	M/LH2O	-0.	4.05203E-05	2.00980E-05	4.47292E-05	3.58164E-06
PROTN	MOLES	-0.	9.96000E-03	5.31100E-02	3.36000E-02	1.14374E 00
	MFRAC	-0.	6.12169E-05	6.58221E-04	7.21914E-05	9.52118E-04
	M/LH2O	-0.	3.39908E-03	3.55478E-02	4.00844E-03	5.28666E-02
HB4	MOLES	-0.	-0.	9.15581E-04	-0.	-0.
	MFRAC	-0.	-0.	1.13473E-05	-0.	-0.
	M/LH2O	-0.	-0.	6.30060E-04	-0.	-0.
HB4O2	MOLES	-0.	-0.	1.55190E-03	-0.	-0.
	MFRAC	-0.	-0.	1.92335E-05	-0.	-0.
	M/LH2O	-0.	-0.	1.06795E-03	-0.	-0.
HB4O4	MOLES	-0.	-0.	1.35175E-03	-0.	-0.
	MFRAC	-0.	-0.	1.30349E-05	-0.	-0.
	M/LH2O	-0.	-0.	7.23767E-04	-0.	-0.
HB4O6	MOLES	-0.	-0.	4.26832E-04	-0.	-0.
	MFRAC	-0.	-0.	5.28995E-06	-0.	-0.
	M/LH2O	-0.	-0.	2.93726E-04	-0.	-0.
HB4O8	MOLES	-0.	-0.	6.66394E-03	-0.	-0.
	MFRAC	-0.	-0.	8.25897E-05	-0.	-0.
	M/LH2O	-0.	-0.	4.58581E-03	-0.	-0.

Table XXII

UREA LOADING PLUS WATER LOADING (RENAL FAILURE)

TABLE XXII QUADRUPLE UREA PLUS 3 LITERS WATER (FIG. 4E)

		AIR	PLASMA	RED CELLS	INTERSTITIAL	INTRACELL
X-BAR		1.00063E 03	1.76835E 02	8.73966E 01	5.05838E 02	1.30555E 03
PH		-0.	7.34382E 00	7.16318E 00	7.36527E 00	6.78714E 00
O2	MOLES	5.27619E 01	1.65299E-04	8.57980E-05	4.72839E-04	1.99205E-03
	MFRAC	5.27089E-02	9.34765E-07	9.81739E-07	9.34765E-07	1.52583E-06
	M/LH2O	0.	5.18781E-05	5.44834E-05	5.18781E-05	8.46815E-05
CO2	MOLES	6.09680E 01	4.92802E-03	2.43556E-03	1.40967E-02	3.63831E-02
	MFRAC	6.09298E-02	2.78680E-05	2.78680E-05	2.78680E-05	2.78680E-05
	M/LH2O	0.	1.54663E-03	1.54653E-03	1.54663E-03	1.54663E-03
N2	MOLES	8.25798E 02	1.46910E-03	1.18079E-03	4.14515E-03	1.76389E-02
	MFRAC	8.25281E-01	8.19463E-06	1.35107E-05	8.19463E-06	1.35107E-05
	M/LH2O	0.	4.54790E-04	7.49822E-04	4.54790E-04	7.49822E-04
H2O	MOLES	6.11180E 01	1.75852E 02	8.59137E 01	5.03025E 02	1.29829E 03
	MFRAC	6.10798E-02	9.94440E-01	9.94440E-01	9.94440E-01	9.94440E-01
	M/LH2O	0.	5.51900E 01	5.51900E 01	5.51900E 01	5.51900E 01
H+	MOLES	-0.	1.44362E-07	1.08148E-07	3.93050E-07	3.84030E-06
	MFRAC	-0.	8.16369E-10	1.23744E-09	7.77028E-10	2.94151E-09
	M/LH2O	-0.	4.53073E-08	6.86783E-08	4.31239E-08	1.63249E-07
OH-	MOLES	-0.	1.68422E-06	5.49146E-07	5.06167E-06	3.45099E-06
	MFRAC	-0.	9.52429E-09	6.28338E-09	1.00065E-08	2.64331E-09
	M/LH2O	-0.	5.28584E-07	3.48719E-07	5.55346E-07	1.46700E-07
CL-	MOLES	-0.	3.14488E-01	1.02540E-01	9.45142E-01	8.72083E-02
	MFRAC	-0.	1.77843E-03	1.17327E-03	1.86867E-03	6.67980E-05
	M/LH2O	-0.	9.87001E-02	6.51146E-02	1.03697E-01	3.70719E-03
NA+	MOLES	-0.	4.47459E-01	3.87437E-02	1.21037E 00	2.15602E-01
	MFRAC	-0.	2.53038E-03	4.43309E-04	2.40862E-03	1.65142E-04
	M/LH2O	-0.	1.40432E-01	2.46030E-02	1.33675E-01	9.16515E-03
K+	MOLES	-0.	1.26200E-02	1.98138E-01	3.36536E-02	3.45409E 00
	MFRAC	-0.	7.13658E-05	2.26711E-03	6.65304E-05	2.64569E-03
	M/LH2O	-0.	3.96070E-03	1.25821E-01	3.69234E-03	1.46832E-01
CA++	MOLES	-0.	8.39741E-03	4.71366E-04	2.10240E-02	2.15519E-02
	MFRAC	-0.	4.74873E-05	5.39341E-06	4.15627E-05	1.65079E-05
	M/LH2O	-0.	2.63548E-03	2.99327E-04	2.30667E-03	9.16165E-04
MG++	MOLES	-0.	3.22841E-03	4.74901E-03	8.42117E-03	2.80560E-01
	MFRAC	-0.	1.82566E-05	5.43478E-05	1.66480E-05	2.14898E-04
	M/LH2O	-0.	1.01322E-03	3.01622E-03	9.23939E-04	1.19265E-02
SO4=	MOLES	-0.	1.46513E-03	3.15156E-04	4.62615E-03	2.15814E-01
	MFRAC	-0.	8.28531E-06	3.50604E-06	9.14553E-06	1.65306E-04
	M/LH2O	-0.	4.59023E-04	2.00130E-04	5.07563E-04	9.17415E-03
HPO4=	MOLES	-0.	3.03513E-03	6.52869E-04	9.58362E-03	1.07903E 00
	MFRAC	-0.	1.71636E-05	7.47018E-06	1.89456E-05	8.26492E-04
	M/LH2O	-0.	9.52557E-04	4.14584E-04	1.05146E-03	4.58691E-02
UREA	MOLES	-0.	5.40185E-02	2.66974E-02	1.54521E-01	3.98813E-01
	MFRAC	-0.	3.05474E-04	3.05474E-04	3.05474E-04	3.05474E-04
	M/LH2O	-0.	1.69534E-02	1.69534E-02	1.69534E-02	1.69534E-02
GLUCOS	MOLES	-0.	1.26047E-02	6.22959E-03	3.60559E-02	9.30593E-02
	MFRAC	-0.	7.12796E-05	7.12796E-05	7.12796E-05	7.12796E-05
	M/LH2O	-0.	3.95591E-03	3.95591E-03	3.95591E-03	3.95591E-03
LACTIC	MOLES	-0.	2.13833E-02	6.97209E-03	6.42641E-02	5.92965E-03
	MFRAC	-0.	1.20923E-04	7.97752E-05	1.27045E-04	4.54187E-06
	M/LH2O	-0.	6.71103E-03	4.42741E-03	7.05081E-03	2.52067E-04
HCO3-	MOLES	-0.	8.78400E-02	3.29444E-02	2.63989E-01	2.07032E-01
	MFRAC	-0.	4.96735E-04	3.76953E-04	5.21885E-04	1.58578E-04
	M/LH2O	-0.	2.75681E-02	2.09233E-02	2.89639E-02	8.80084E-03
H2CO3	MOLES	-0.	7.00846E-06	3.46378E-06	2.00478E-05	5.17428E-05
	MFRAC	-0.	3.96328E-08	3.96328E-08	3.96328E-08	3.96328E-08
	M/LH2O	-0.	2.19957E-06	2.19957E-06	2.19957E-06	2.19957E-06
CO3=	MOLES	-0.	1.09884E-04	2.71885E-05	3.46059E-04	7.18780E-05
	MFRAC	-0.	6.21395E-07	3.11093E-07	6.85910E-07	5.50556E-08
	M/LH2O	-0.	3.44865E-05	1.72652E-05	3.80670E-05	3.05551E-06
PROTN	MOLES	-0.	9.96000E-03	5.31130E-02	3.36000E-02	1.14374E 00
	MFRAC	-0.	5.63238E-05	6.07690E-04	6.64245E-05	8.76058E-04
	M/LH2O	-0.	3.12589E-03	3.37259E-02	3.68646E-03	4.86200E-02
HB4	MOLES	-0.	-0.	1.33363E-03	-0.	-0.
	MFRAC	-0.	-0.	1.18269E-05	-0.	-0.
	M/LH2O	-0.	-0.	6.56375E-04	-0.	-0.
HB4O2	MOLES	-0.	-0.	1.58104E-03	-0.	-0.
	MFRAC	-0.	-0.	1.92346E-05	-0.	-0.
	M/LH2O	-0.	-0.	1.36749E-03	-0.	-0.
HB4O4	MOLES	-0.	-0.	1.09314E-03	-0.	-0.
	MFRAC	-0.	-0.	1.25078E-05	-0.	-0.
	M/LH2O	-0.	-0.	6.34153E-04	-0.	-0.
HB4O6	MOLES	-0.	-0.	4.25661E-04	-0.	-0.
	MFRAC	-0.	-0.	4.87045E-06	-0.	-0.
	M/LH2O	-0.	-0.	2.70303E-04	-0.	-0.
HB4O8	MOLES	-0.	-0.	6.37654E-03	-0.	-0.
	MFRAC	-0.	-0.	7.29609E-05	-0.	-0.
	M/LH2O	-0.	-0.	4.04923E-03	-0.	-0.

HEMORRHAGE-FIRST APPROXIMATION

In a preliminary experiment to demonstrate the effect of loss of blood, one-fifth of the blood was removed from the mathematical model, Fig. 4F and Table XXIII. Since blood of identical composition to that present was removed, there is no observable change in interstitial or intracellular composition* in the model. Obviously, this result is not that expected in the body where profound electrolyte and fluid shifts occur [2,29].

A better mathematical approximation to hemorrhage may be had by postulating that initially, before the body compensatory mechanisms occur, the fluid shifts begin as a result of loss of pressure in the capillary bed. Under the influence of pressure gradients, fluid and electrolyte will move across compartment boundaries, but this model does not yet explicitly incorporate variable pressure effects.

HEMORRHAGE WITH NaCl ADDITION

As an additional test, one liter of isotonic saline was added to the hemorrhage model above. This amount of fluid very nearly restores the volume loss of blood, but obviously notable shifts in fluid must be expected (Fig. 4G

*See Bland [29] and the section on Isotonic Contraction above.

Table XXIII

HEMORRHAGE-FIRST APPROXIMATION

TABLE XXIII DEDUCT 1/5 PLASMA PLUS RED CELLS (FIG. 4F)

		AIR	PLASMA	RED CELLS	INTERSTITIAL	INTRACELL
X-BAR		1.00061E 03	1.30158E 02	6.51952E 01	4.65511E 02	1.20006E 03
PH		-0.	7.38335E 00	7.20251E 00	7.40478E 00	6.82855E 00
O2	MOLES	5.27411E 01	1.21667E-04	6.39633E-05	4.35142E-04	1.83109E-03
	MFRAC	5.27088E-02	9.34762E-07	9.81706E-07	9.34762E-07	1.52583E-06
	M/LH2O	0.	5.18093E-05	5.44952E-05	5.18093E-05	8.46997E-05
CO2	MOLES	6.09679E 01	3.62729E-03	1.81576E-03	1.29730E-02	3.34437E-02
	MFRAC	6.09305E-02	2.78683E-05	2.78683E-05	2.78683E-05	2.78683E-05
	M/LH2O	0.	1.54699E-03	1.54699E-03	1.54699E-03	1.54699E-03
N2	MOLES	8.25800E 02	1.06662E-03	8.80306E-06	3.81479E-03	1.62139E-02
	MFRAC	8.25294E-01	8.19476E-06	1.35139E-05	8.19476E-06	1.35109E-05
	M/LH2O	0.	4.54897E-04	7.49990E-04	4.54897E-04	7.49990E-04
H2O	MOLES	6.11038E 01	1.29407E 02	6.47788E 01	4.62821E 02	1.19313E 03
	MFRAC	6.10664E-02	9.94223E-01	9.94223E-01	9.94223E-01	9.94223E-01
	M/LH2O	0.	5.51900E 01	5.51900E 01	5.51900E 01	5.51900E 01
H+	MOLES	-0.	9.69927E-08	7.36301E-08	3.30188E-07	3.20825E-06
	MFRAC	-0.	7.49189E-10	1.13037E-09	7.09322E-10	2.67340E-09
	M/LH2O	-0.	4.13660E-08	6.27311E-08	3.93739E-08	1.48402E-07
OH-	MOLES	-0.	1.35778E-06	4.48195E-07	5.10179E-06	3.48951E-06
	MFRAC	-0.	1.04318E-08	6.87888E-09	1.09596E-08	2.90777E-09
	M/LH2O	-0.	5.79074E-07	3.81852E-07	5.08372E-07	1.61412E-07
CL-	MOLES	-0.	2.51316E-01	8.29578E-02	9.46305E-01	8.74109E-02
	MFRAC	-0.	1.93085E-03	1.27323E-03	2.02854E-03	7.28369E-05
	M/LH2O	-0.	1.07183E-01	7.06781E-02	1.12605E-01	4.06332E-03
NA+	MOLES	-0.	3.58038E-01	3.14143E-02	1.21894E 00	2.14510E-01
	MFRAC	-0.	2.75078E-03	4.82146E-04	2.61850E-03	1.78749E-04
	M/LH2O	-0.	1.52698E-01	2.67643E-02	1.45395E 01	9.92266E-03
K+	MOLES	-0.	1.01398E-02	1.51320E-01	3.30009E-02	3.45082E 00
	MFRAC	-0.	7.79033E-05	2.47596E-03	7.26275E-05	2.87553E-03
	M/LH2O	-0.	4.32467E-03	1.37441E-01	4.03160E-03	1.59623E-01
CA++	MOLES	-0.	6.74448E-03	3.83006E-06	2.11135E-02	2.14300E-02
	MFRAC	-0.	5.18174E-05	5.99365E-06	4.53556E-05	1.78574E-05
	M/LH2O	-0.	2.87642E-03	3.26996E-06	2.51772E-03	9.91275E-04
MG++	MOLES	-0.	2.60387E-03	3.08679E-03	8.49922E-03	2.80364E-01
	MFRAC	-0.	2.00207E-05	5.96543E-05	1.02578E-05	2.33624E-04
	M/LH2O	-0.	1.11136E-03	3.31169E-03	1.01351E-03	1.29606E-02
SO4=	MOLES	-0.	1.16327E-03	2.53209E-04	4.59208E-03	2.15895E-01
	MFRAC	-0.	8.93737E-06	3.80625E-06	9.86661E-06	1.79869E-04
	M/LH2O	-0.	4.96119E-04	2.15728E-04	5.47591E-04	9.98488E-03
HPO4=	MOLES	-0.	2.40954E-03	5.24403E-04	9.51178E-03	1.07912E 00
	MFRAC	-0.	1.85124E-05	8.04975E-06	2.04330E-05	8.99215E-04
	M/LH2O	-0.	1.02763E-03	4.46847E-04	1.13425E-03	4.99160E-02
UREA	MOLES	-0.	8.64357E-03	4.32683E-03	3.09136E-02	7.96939E-02
	MFRAC	-0.	6.64080E-05	6.64080E-05	6.64080E-05	6.64080E-05
	M/LH2O	-0.	3.68636E-03	3.68636E-03	3.68636E-03	3.68636E-03
GLUCOS	MOLES	-0.	1.00845E-02	5.04014E-03	3.60671E-02	9.29796E-02
	MFRAC	-0.	7.74787E-05	7.74787E-05	7.74787E-05	7.74787E-05
	M/LH2O	-0.	4.30089E-03	4.30089E-03	4.30089E-03	4.30089E-03
LACTIC	MOLES	-0.	1.70880E-02	5.64064E-03	6.42072E-02	5.94363E-02
	MFRAC	-0.	1.31206E-04	8.65724E-05	1.37929E-04	4.95259E-06
	M/LH2O	-0.	7.28779E-03	4.80569E-03	7.65651E-03	2.74922E-04
HCO3-	MOLES	-0.	7.08153E-02	2.68885E-02	2.66085E-01	2.09365E-01
	MFRAC	-0.	5.44070E-04	4.12683E-04	5.71597E-04	1.74465E-04
	M/LH2O	-0.	3.02017E-02	2.29063E-02	3.17298E-02	9.68357E-03
H2CO3	MOLES	-0.	9.15748E-06	2.50179E-06	1.84697E-05	4.75521E-05
	MFRAC	-0.	3.96246E-08	3.96246E-08	3.96246E-08	3.96246E-08
	M/LH2O	-0.	2.19959E-06	2.19959E-06	2.19959E-06	2.19959E-06
CO3=	MOLES	-0.	9.70408E-05	2.42990E-05	3.83105E-04	7.99703E-03
	MFRAC	-0.	7.45620E-07	3.72941E-07	8.22978E-07	6.66384E-06
	M/LH2O	-0.	4.13899E-05	2.07022E-05	4.56841E-05	3.69914E-04
PROTN	MOLES	-0.	7.96000E-03	4.26880E-02	3.36000E-02	1.14374E 00
	MFRAC	-0.	6.12177E-05	6.52104E-04	7.21788E-05	9.53066E-04
	M/LH2O	-0.	3.39824E-03	3.61988E-02	4.00670E-03	5.29053E-02
HB4	MOLES	-0.	-0.	7.15453E-04	-0.	-0.
	MFRAC	-0.	-0.	1.09830E-05	-0.	-0.
	M/LH2O	-0.	-0.	6.39549E-04	-0.	-0.
HB4O2	MOLES	-0.	-0.	1.22227E-03	-0.	-0.
	MFRAC	-0.	-0.	1.87593E-05	-0.	-0.
	M/LH2O	-0.	-0.	1.09134E-03	-0.	-0.
HB4O4	MOLES	-0.	-0.	8.34899E-04	-0.	-0.
	MFRAC	-0.	-0.	1.28140E-05	-0.	-0.
	M/LH2O	-0.	-0.	7.11314E-04	-0.	-0.
HB4O6	MOLES	-0.	-0.	3.41534E-04	-0.	-0.
	MFRAC	-0.	-0.	5.24130E-06	-0.	-0.
	M/LH2O	-0.	-0.	2.90953E-04	-0.	-0.
HB4O8	MOLES	-0.	-0.	5.37388E-03	-0.	-0.
	MFRAC	-0.	-0.	8.24781E-05	-0.	-0.
	M/LH2O	-0.	-0.	4.57862E-03	-0.	-0.

and Table XXIV) since the electrolyte composition is not identical to that lost.

Intracellular volume is down from normal, with most of the loss in red cells. Muscle tissue volume is only off 0.5 per cent while red cells have lost more than 20 per cent of normal volume. Surprisingly, the analog of interstitial edema is present in that interstitial compartment volume is increased, but plasma volume is below normal although above the volume in simple hemorrhage. Consequently, the hematocrit is down only 3 per cent from normal whole-body ratio. Na^+ mole fraction is very near normal in all compartments; K^+ mole fraction is up slightly (2 per cent) in extracellular spaces; and Cl^- mole fraction is high in all compartments since more was replaced than was removed. There is a slight acidosis. Generally, except for the 10 per cent increase in interstitial volume at the expense of the whole blood, the mathematical hemorrhage treated with saline gives a mathematical result very similar to normal body distribution.

Obviously, these last three experiments require much additional work in conjunction with a clinical laboratory. These rudimentary experiments only illustrate the nature of the experiments which a mathematical simulation makes possible.

Table XXIV

HEMORRHAGE PLUS FLUIDS

TABLE XXIV ADD 1 LITER ISOTONIC NACL TO HEMORAGE (FIG. 46)

		AIR	PLASMA	RED CELLS	INTERSTITIAL	INTRACELL
X-BAR		1.00061E 03	1.42175E 02	6.57446E 01	5.11891E 02	1.19658E 03
PH		-0.	7.36051E 00	7.18193E 00	7.38013E 00	6.80654E 00
O2	MOLES	5.27415E 01	1.32901E-04	6.45425E-05	4.78501E-04	1.82579E-03
	MFRAC	5.27093E-02	9.34771E-07	9.81716E-07	9.34771E-07	1.52584E-06
	M/LH2O	0.	5.18895E-05	5.44954E-05	5.18895E-05	8.47001E-05
CO2	MOLES	6.09658E 01	3.96204E-03	1.83213E-03	1.42651E-02	3.33455E-02
	MFRAC	6.09285E-02	2.78674E-05	2.78674E-05	2.78674E-05	2.78674E-05
	M/LH2O	0.	1.54693E-03	1.54693E-03	1.54693E-03	1.54693E-03
N2	MOLES	8.25800E 02	1.16509E-03	8.88269E-04	4.19483E-03	1.61668E-02
	MFRAC	8.25296E-01	8.19478E-06	1.35139E-05	8.19478E-06	1.35109E-05
	M/LH2O	0.	4.54895E-04	7.49996E-04	4.54895E-04	7.49996E-04
H2O	MOLES	6.11040E 01	1.41354E 02	6.53651E 01	5.08936E 02	1.18967E 03
	MFRAC	6.10667E-02	9.94228E-01	9.94228E-01	9.94228E-01	9.94228E-01
	M/LH2O	0.	5.51900E 01	5.51900E 01	5.51900E 01	5.51900E 01
H+	MOLES	-0.	1.11648E-07	7.79016E-08	3.84290E-07	3.36528E-06
	MFRAC	-0.	7.85427E-10	1.18491E-09	7.50728E-10	2.81242E-09
	M/LH2O	-0.	4.35994E-08	6.57750E-08	4.16732E-08	1.56119E-07
OH-	MOLES	-0.	1.40716E-06	4.31320E-07	5.30055E-06	3.30740E-06
	MFRAC	-0.	9.89739E-09	6.56055E-09	1.03549E-08	2.76405E-09
	M/LH2O	-0.	5.49408E-07	3.64179E-07	5.74802E-07	1.53433E-07
CL-	MOLES	-0.	2.81925E-01	8.64154E-02	1.06197E 00	8.96786E-02
	MFRAC	-0.	1.98295E-03	1.31441E-03	2.07460E-03	7.49459E-05
	M/LH2O	-0.	1.10074E-01	7.29635E-02	1.15182E-01	4.16028E-03
NA+	MOLES	-0.	3.90067E-01	3.14514E-02	1.34246E 00	2.12922E-01
	MFRAC	-0.	2.74357E-03	4.78387E-04	2.62256E-03	1.77943E-04
	M/LH2O	-0.	1.52297E-01	2.65555E-02	1.45579E-01	9.87767E-03
K+	MOLES	-0.	1.11107E-02	1.62444E-01	3.74501E-02	3.44509E 00
	MFRAC	-0.	7.81483E-05	2.47084E-03	7.31634E-05	2.87912E-03
	M/LH2O	-0.	4.33804E-03	1.37157E-01	4.06117E-03	1.59821E-01
CA++	MOLES	-0.	6.97704E-03	3.62976E-04	2.21720E-02	2.01598E-02
	MFRAC	-0.	4.90737E-05	5.52100E-06	4.33139E-05	1.68479E-05
	M/LH2O	-0.	2.72410E-03	3.06473E-04	2.40437E-03	9.35232E-04
MG++	MOLES	-0.	2.85331E-03	3.89073E-03	9.44707E-03	2.79165E-01
	MFRAC	-0.	2.00690E-05	5.91794E-05	1.84552E-05	2.33303E-04
	M/LH2O	-0.	1.11404E-03	3.28537E-03	1.02446E-03	1.29507E-02
SO4=	MOLES	-0.	1.26657E-03	2.57339E-04	4.99150E-03	2.15348E-01
	MFRAC	-0.	8.90856E-06	3.91423E-06	9.75111E-06	1.79970E-04
	M/LH2O	-0.	4.94518E-04	2.17200E-04	5.41288E-04	9.99021E-03
HPO4=	MOLES	-0.	2.62708E-03	5.33764E-04	1.03532E-02	1.07805E 00
	MFRAC	-0.	1.84778E-05	8.11874E-06	2.02254E-05	9.00942E-04
	M/LH2O	-0.	1.02571E-03	4.50679E-04	1.12272E-03	5.00117E-02
UREA	MOLES	-0.	9.16811E-03	4.23953E-03	3.30092E-02	7.71611E-02
	MFRAC	-0.	6.44848E-05	6.44848E-05	6.44848E-05	6.44848E-05
	M/LH2O	-0.	3.57958E-03	3.57958E-03	3.57958E-03	3.57958E-03
GLUCOS	MOLES	-0.	1.06965E-02	4.94628E-03	3.85120E-02	9.00243E-02
	MFRAC	-0.	7.52349E-05	7.52349E-05	7.52349E-05	7.52349E-05
	M/LH2O	-0.	4.17632E-03	4.17632E-03	4.17632E-03	4.17632E-03
LACTIC	MOLES	-0.	1.72271E-02	5.28043E-03	6.48919E-02	5.47983E-03
	MFRAC	-0.	1.21169E-04	8.03173E-05	1.26769E-04	4.57958E-06
	M/LH2O	-0.	6.72612E-03	4.45865E-03	7.03703E-03	2.54215E-04
HCO3-	MOLES	-0.	7.33882E-02	2.58753E-02	2.76442E-01	1.98413E-01
	MFRAC	-0.	5.16183E-04	3.93572E-04	5.40042E-04	1.65817E-04
	M/LH2O	-0.	2.86535E-02	2.18674E-02	2.99779E-02	9.20460E-03
H2CO3	MOLES	-0.	5.63347E-06	2.50503E-06	2.02829E-05	4.74126E-05
	MFRAC	-0.	3.96235E-08	3.96235E-08	3.96235E-08	3.96235E-08
	M/LH2O	-0.	2.19952E-06	2.19952E-06	2.19952E-06	2.19952E-06
C3=	MOLES	-0.	9.54223E-05	2.23012E-05	3.76055E-04	7.20477E-05
	MFRAC	-0.	6.71162E-07	3.39239E-07	7.34640E-07	6.02114E-08
	M/LH2O	-0.	3.72565E-05	1.88296E-05	4.07802E-05	3.34236E-06
PROTN	MOLES	-0.	7.96800E-03	4.24880E-02	3.36000E-02	1.14376E 00
	MFRAC	-0.	5.60437E-05	6.46259E-04	6.56390E-05	9.55843E-04
	M/LH2O	-0.	3.11101E-03	3.58741E-02	3.64365E-03	5.30592E-02
HB4	MOLES	-0.	-0.	7.71403E-04	-0.	-0.
	MFRAC	-0.	-0.	1.17333E-05	-0.	-0.
	M/LH2O	-0.	-0.	6.51322E-04	-0.	-0.
HB4O2	MOLES	-0.	-0.	1.28683E-03	-0.	-0.
	MFRAC	-0.	-0.	1.95428E-05	-0.	-0.
	M/LH2O	-0.	-0.	1.08683E-03	-0.	-0.
HB4O4	MOLES	-0.	-0.	8.55646E-04	-0.	-0.
	MFRAC	-0.	-0.	1.30147E-05	-0.	-0.
	M/LH2O	-0.	-0.	7.22451E-04	-0.	-0.
HB4O6	MOLES	-0.	-0.	3.41221E-04	-0.	-0.
	MFRAC	-0.	-0.	5.19010E-06	-0.	-0.
	M/LH2O	-0.	-0.	2.88104E-04	-0.	-0.
HB4O8	MOLES	-0.	-0.	5.23489E-03	-0.	-0.
	MFRAC	-0.	-0.	7.96247E-05	-0.	-0.
	M/LH2O	-0.	-0.	4.42000E-03	-0.	-0.

VII. CONCLUSIONS

A mathematical model for computing the fluid and electrolyte distribution in the principal body compartments of a young, male human has been discussed. This report deals with the computed distribution resulting from chemical mass action laws and electrochemical forces--i.e., pressure and temperature are presumed constant thoughout, there is no compensatory hormonal regulation, and, most important, there is no kidney. Nevertheless, the model yields a great deal of insight regarding fluid balance.

Certainly the model is not complete; considerable detail must be added concerning, for example, protein chemistry and the behavior of double-valent ions. However, the major effects appear to be present in that the model responds in rational ways over a considerable chemical stress range.

Validation of the model proceeds along two lines: the qualitative responses of the system to chemical stress are compared with similar experiments reported in the literature; and the quantitative aspects are tested against nephrectomized animals. Generally, these results show that even this simple model gives the correct qualitative responses and reasonable quantitative answers.

The model will improve in validity as future research findings are incorporated, i.e., adding chemical detail and subtlety to the flexible format. The details of the mathematical model are, however, so numerous that few laboratory reports contain enough data to verify all aspects of the model; e.g., intracellular Na^+ concentration under various stresses. There are two consequences of this. First, some of the nonmeasureable data (e.g., hemoglobin carbamino compounds) must be accepted by inference; if the response of the system is correct in the main, measurable variables, and if the carbamino-hemoglobin system, say, behaves properly in isolated, small sub-experiments, then it may be presumed that the small system is functioning properly when incorporated into the large model. Secondly, new laboratory experiments had to be planned with more detailed goals. But, this illustrates one of the principle purposes of the model: to interact as a complex tool with the laboratory. The work of Bradham, et al. [1], demonstrates this usefulness.

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